



HEART.

HEART.

A JOURNAL FOR THE STUDY OF THE CIRCULATION.

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ERRATA.

Vol. III, page 56, line 16; for "50" read "5."

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HEART-BLOCK FROM DRUGS OF THE DIGITALIS GROUP. THE COMPARATIVE EFFECTS OF DIGITALIS, STROPHANTHUS, SQUILL AND APOCYNUM.

BY J. DAVENPORT WINDLE.

(*Southall.*)

It is well established that the administration of digitalis causes impairment of conductivity and heart-block in some patients. This happens most frequently in cases of old rheumatic mitral stenosis, and the degenerative heart lesions associated with arterial disease in which the function of the bundle is already impaired by structural changes as evidenced by a lengthened *a-c* interval. In such cases, small quantities of digitalis increase the duration of the intersystolic interval and a slight degree of heart-block commonly results, a ventricular intermission recurring after a variable number of regular beats, and at times a 2:1 or 3:1 rhythm ensuing. In patients showing primary heart-block to this degree, digitalis usually increases the grade of block. In cases which show no evidence of primarily impaired conductivity, digitalis does not readily depress this function as a rule. At times, as a quickly acting heart slows towards the normal rate as a result of its employment, the *a-c* interval lengthens and, exceptionally, a 2:1 rhythm may follow; generally, however, this occurs only after large quantities of the drug have been taken; a higher degree of heart-block is but rarely observed, and complete block from digitalis is very exceptional. I have noticed however in patients with arterio-sclerosis that small quantities of digitalis may produce heart-block when such an effect would not be expected from the character of the jugular tracing. In one such case under my observation, in which the *a-c* interval was under $\frac{1}{2}$ sec., as little as six doses of 15 minims of the tincture of digitalis caused a 2:1 rhythm on several occasions. I have observed the same susceptibility in other cases of arterio-cardio-sclerosis.

In the illustrative case described in this paper, the comparative degrees of heart-block provoked by the administration of digitalis, strophanthus, squill and apocynum are given; the comparison has been instituted in one and the same patient.

There was no evidence of disturbed conduction before the administration of drugs began, or after their effects had passed off. Varying degrees of impaired conductivity and transient complete dissociation of auricular and ventricular rhythms occurred under the influence of the drugs mentioned.

except apocynum. In some of the records it is questionable whether the failure of the ventricle to respond to auricular impulses was wholly due to impairment of conduction or to impairment of some other function.

History.

The patient, a tall spare woman, aged 53 years, is known to have had mitral valvular disease for many years. Her health has always been good, and she has had no heart symptoms until the present illness, for which she first came under observation on March the 15th, 1910. For some time prior to this date she had been somewhat breathless after exertion; three weeks ago urgent dyspnoea together with severe pain "over the heart and in the left shoulder" occurred; the feet and legs have since been swollen.

The patient comes of a rheumatic stock, and two of her children have had rheumatic fever. She has had several attacks of rheumatic fever, the last at 20 years of age.

Condition, March the 15th, 1910.

The breathing is quick and short, she is unable to lie down in bed; the pulse is at 100 per minute and is regular in rhythm, the beats being abrupt and dicrotic; the systolic blood pressure is 115. The chest is long and narrow; the heart's impulse is in the 5th space, $5\frac{1}{2}$ inches to the left of the middle line, and is feeble and diffuse. No precordial thrill is palpable. The heart's dulness is $5\frac{1}{2}$ inches to the left of the middle line and $1\frac{1}{2}$ inches to the right in the 4th space; it extends upwards to the left third rib. On auscultation, a long blowing systolic murmur, replacing the first sound, is heard at the apex; it is conducted outwards and heard at the back. The second sound is clear and no murmur is heard during diastole; the sounds at the base of the heart are clear, the second sound in the pulmonary area is accentuated. Pulsation is evident in the superficial, but not in the deep jugular veins; the liver is not palpable; there is no ascites; the feet and legs are very swollen. The urine is scanty; its specific gravity is 1025 and it is loaded with albumin.

Subsequent history.

With complete rest in bed, together with administration of digitalis, the symptoms gradually cleared up, and by the 12th day of treatment the heart had diminished in size; the breathing was normal, the dropsy was gone and the copious urine contained only a trace of albumin. Pronounced symptoms of heart failure recurred on several occasions, and bodily weakness became progressively greater. The patient died in a comatose condition after an attack of hemiplegia $10\frac{1}{2}$ months subsequent to the first onset of heart symptoms.

Administration of digitalis.

The administration of digitalis was begun on March the 15th, 1910, 15 minims being given three times a day.

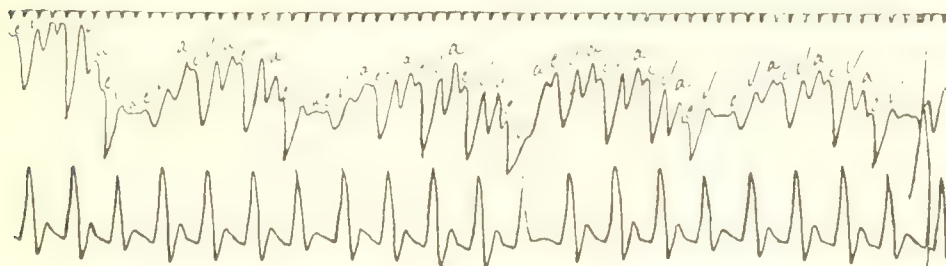


Fig. 1. Tracing of jugular and radial pulses before digitalis. Pulse rate 100 per min.. The *a-c* interval is under $\frac{1}{2}$ sec..

Fig. 1 is a record of jugular and radial pulses before digitalis was given : it shows no evidence of impaired conductivity : the *a-c* interval is less than $\frac{1}{2}$ sec. : the pulse continued regular up to the 12th day of observation when an occasional intermission was noticed, suggesting an extrasystole too feeble to send a wave to the wrist. Against this were the facts that the heart-beat intermitted with the radial pulse, and no sounds could be heard over the heart during these pauses. The nature of the irregularity is made clear in Fig. 2.

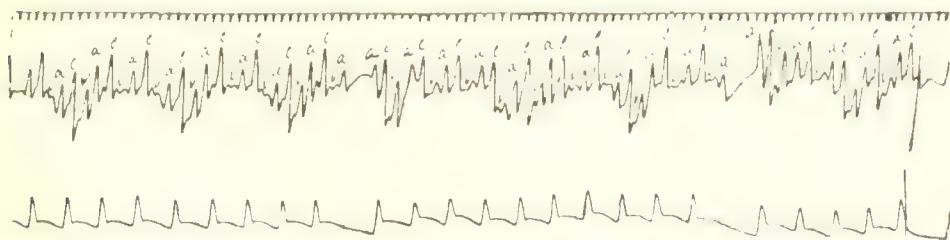


Fig. 2. Taken on the 12th day, after 540 minims of digitalis. Pulse rate about 75 per min.. Sinus arrhythmia is present. The *a-c* interval varies from $\frac{1}{2}$ sec. to $\frac{3}{4}$ sec. in the beats immediately preceding the intermission.

In Fig. 2 the intermissions result from the blocking of auricular impulses. Impairment of conductivity is shown by the increased duration of the *a-c* interval which is nearly $\frac{3}{4}$ sec. in the beats immediately preceding the blocked auricular contractions. The depression of conductivity cannot be ascribed to increased rate of the auricle, for it is beating less frequently, but its rhythm is not now quite regular, variations in length of the inter-auricular periods occurring here and there (compare Fig. 1).

Although the changes in auricular rate are slight, they suffice to influence the conduction of impulses, the *a-c* interval lengthening out with the shorter

periods, and the contrary. In the beat immediately preceding the first intermission the *a-c* interval is approximately $\frac{1}{2}$ sec. and the next auricular stimulus fails to pass; with the succeeding beat conductivity is restored and the stimulus passes in the normal time, but its rate of transmission is again delayed, and ventricular intermission recurs after the tenth beat. These changes were fairly constant over long tracings. Similar events are more clearly shown in Fig. 11.

The patient's condition at this time was in every way satisfactory and the digitalis was continued in the same doses. On the 13th day a coupled rhythm of the pulse was almost constantly present when the patient was quiet.

To the finger the character of the radial pulse closely resembled that due to regularly recurring extrasystoles, and this was to some extent supported by auscultation, coupled beats being followed by a long pause, but the sounds with the second beat, instead of being shorter and more feeble than those of the first beat which is usual in extrasystole, were of the same strength and duration. The nature of the irregularity could not be certainly determined apart from the jugular tracing and this showed that the bigeminy was caused by blocking of every third auricular impulse. On slight exertion the pulse quickened and became regular, but quickly took on the bigeminal rhythm

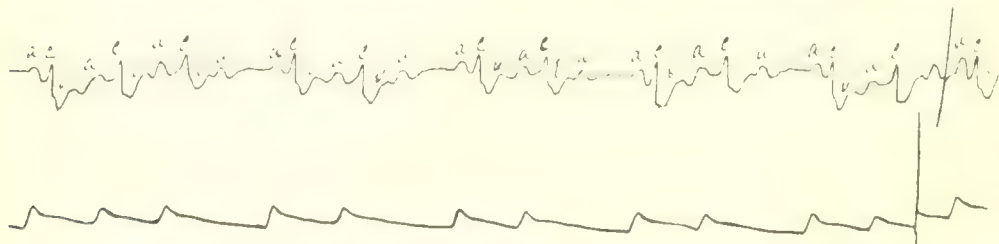


FIG. 3. Taken on the 13th day, immediately after slight exercise and when 10 drachms tinct. digitalis had been taken. The *a-c* interval after the short pulse periods is double the duration of that after the long pauses.

again. This is shown in Fig. 3 which was obtained within two minutes after quickening of the pulse, induced by the patient sitting up and lying down in bed a few times, had occurred.

The *a-c* interval after the short pulse periods is double the duration of that after the long pauses.

On the 14th day, after 10½ drachms of tincture of digitalis had been taken, vomiting ensued; otherwise the general condition was very satisfactory. The symptom quickly subsided after a few 20 grain doses of carbonate of bismuth had been given.

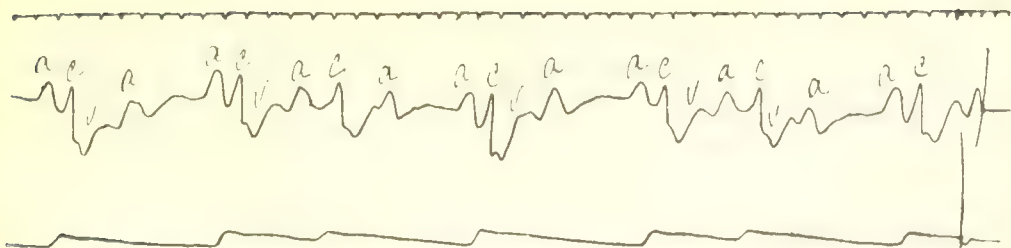


Fig. 4. Shows an alternate bigeminy : the *a-c* interval is fully $\frac{1}{4}$ sec. after the short pulse periods : $10\frac{1}{2}$ drachms tinct. digitalis had been taken when this record was obtained.

Fig. 4 shows a polygraph tracing taken on this day : further depression of conductivity is shown : a period of 1 : 1 rhythm being regularly followed by two periods of 2 : 1 rhythm, giving rise to an alternate bigeminy.

From left to right the venous curve shows the following events. The first *a* wave is followed by a ventricular systole : the next auricular impulse fails to get through. The third auricular beat as a result of the prolonged rest is transmitted at the normal rate. The fourth auricular systole is also transmitted to the ventricle, but, as the result of the shorter time allowed for the recovery of conductivity, this stimulus passes at a much slower rate, the duration of the *a-c* interval is doubled. The transmission of this impulse so impairs conductivity that it is not restored by the time the next auricular stimulus occurs and this fails to get through.

Administration of strophanthus.

The patient continued to improve and was soon sufficiently well to go away for a change. She was from home about three months : during her absence, an attack of hemiplegia with aphasia occurred, probably from embolus. Three weeks before returning home, symptoms of heart failure recurred, and when she again came under my care the condition was much the same as on the first occasion. Tincture of strophanthus, in doses of 15 minims, was administered four times a day and was continued in the same doses for thirteen days.

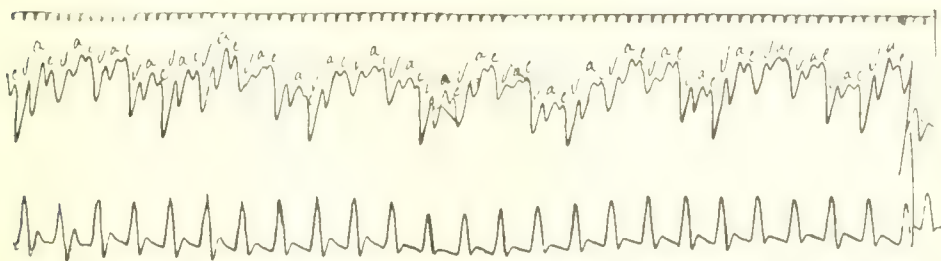


Fig. 5. Record of radial and jugular pulses, before the administration of strophanthus. Pulse rate 75 per min.. The *a-c* interval is under $\frac{1}{4}$ sec..

Fig. 5 is the record taken before strophanthus, the rhythm is regular and the rate 75 per minute, the *a-c* interval being under $\frac{1}{4}$ sec.. It is identical

with Fig. 1. The first change in the pulse was noticed on the 19th day after administration; that is to say, after 540 minims had been taken.

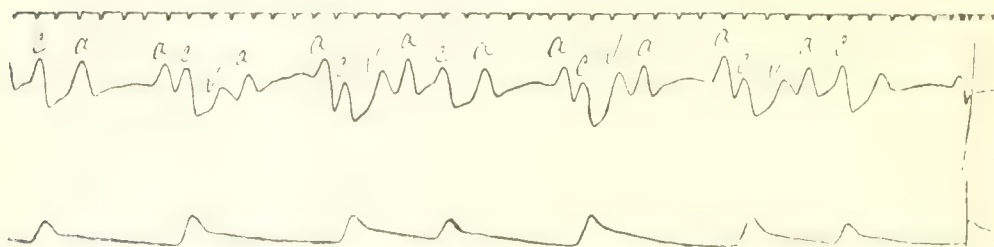


Fig. 6. Obtained on the ninth day, after 540 minims tinct. Strophanthus had been given. An alternate bigeminy is present. Compare Fig. 4 under digitalis.

The ventricle showed an alternate bigeminy (Fig. 6); in this connection it is interesting to compare Fig. 4 (under digitalis) in which the rhythm is the same and the rates of the bigeminal and single beats are equal; the duration of the *a-c* interval after the shorter pulse periods is approximately $\frac{1}{10}$ sec. less under strophanthus. Two days later, the pulse was almost perfectly regular when the patient was quiet.

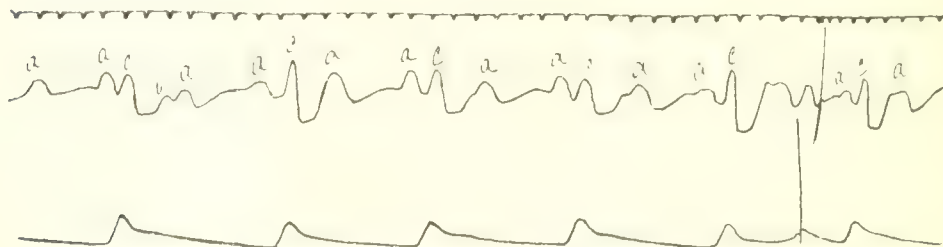


Fig. 7. Taken two days after Fig. 6. Shows a continuous 2:1 heart block.

Fig. 7 was taken at this time; the radial pulse was 43 per minute, the heart's impulse and sounds corresponded; without knowledge of the existing condition, heart-block would probably not have been thought of; and at first sight it is not suggested by the radial and jugular tracing, the *a-c* interval is normal and the venous curve closely resembles an ordinary *a-c-v* pulsation: measurement however clearly shows a condition of 2:1 heart-block, *a* and *c* fusing, and where they fall together the wave is exaggerated. Moreover, slowing of the ventricle under drugs of the digitalis group, to a rate of 43 per minute and with the normal pacemaker active, has perhaps never been observed apart from heart-block.

The symptoms at this time were much improved; the patient experienced slight nausea, but there was no vomiting. It was deemed expedient to continue the administration of strophanthus in the same doses but at longer intervals; 15 minims, thrice daily, were prescribed. She was not

seen again until the 13th day; by this time approximately 12 drachms of tincture of strophanthus had been taken, somewhat severe vomiting had occurred, but otherwise the condition was much the same. The heart's action was irregular.

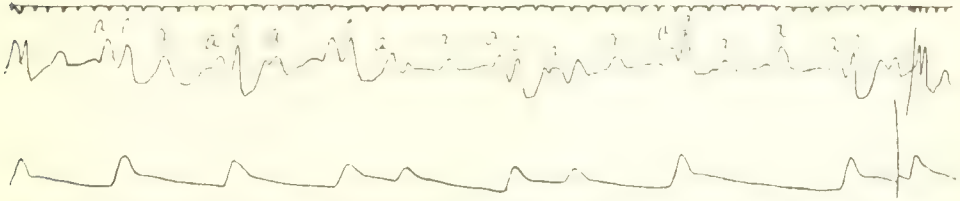


Fig. 8. Taken on the thirteenth day, after 12 drachms tinct. strophanthus. Shows 2:1 and 3:1 rhythms. There is no variation in the *a-c* interval with the bigeminal beats.

The curves are complex (Fig. 8); a notable feature in the absence of any evidence of impairment of conductivity, the *a-c* interval, corresponding to the bigeminal beat of the radial pulse, does not exceed $\frac{1}{2}$ sec.; thus there is no evidence of sufficient depression of conductivity to explain the blocking of stimuli from this cause. We should expect the interval to be longer than $\frac{1}{2}$ sec. after the transmission of two successive stimuli, that is to say, with the second beat of the bigeminy (compare Fig. 4).

The administration of squill.

After the cessation of strophanthus the patient continued fairly well for about six weeks, and was able to get about the house comfortably; symptoms of failure again gradually ensued and when she came under observation for this attack, dyspnoea was urgent; the dropsy was more severe and extensive than before; the urine was very scanty and was loaded

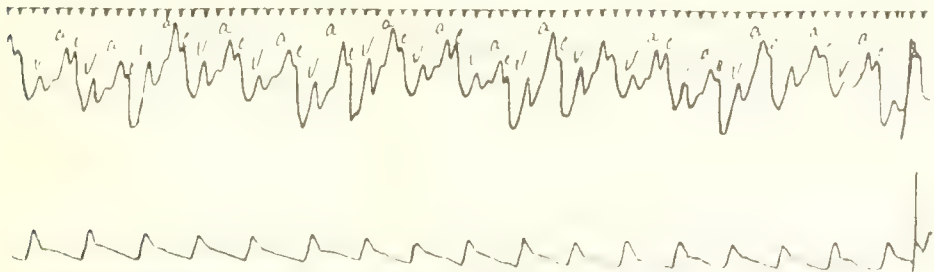


Fig. 9. Taken before the administration of squill. Pulse rate 75 per min.; *a-c* interval normal.

with albumin. The condition of the pulse is shown in Fig. 9, a curve taken before the administration of squill was begun.

The drug was given four times a day in doses of 30 minims without intermission. Improvement was rapid; no vomiting occurred at any time, on the 10th day slight nausea was experienced when squill was discontinued.

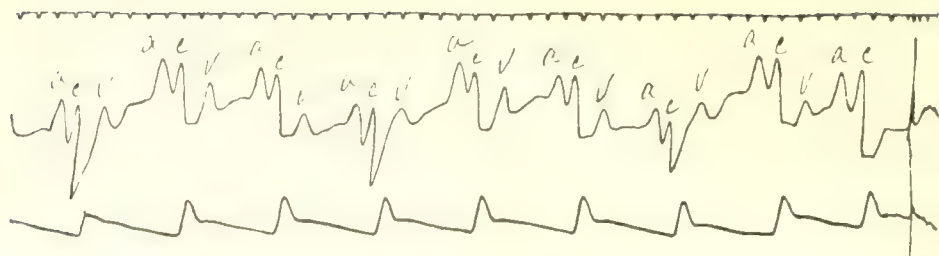


Fig. 10. Shows a regular slowing of the pulse to 55 per min., $a-c$ interval full $\frac{1}{2}$ sec., After 480 minims squill.

The first effect is shown in this figure (Fig. 10), in which there is a regular slowing of the heart to 55 a minute with slight delay in conductivity, the $a-c$ interval being a full $\frac{1}{2}$ sec.. This tracing was obtained after 480 minims had been taken; two days later another tracing (Fig. 11) was taken.

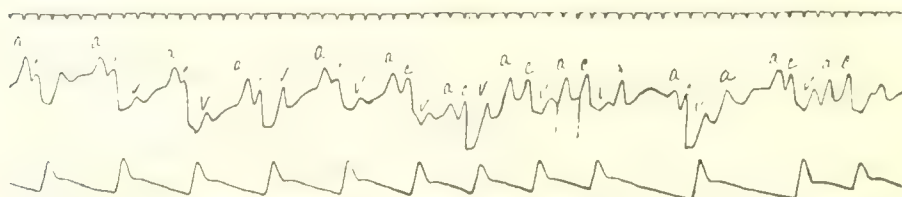


Fig. 11. Taken two days after Fig. 10. The regular rhythm in the first part of the tracing is succeeded by four quicker beats, and the $a-c$ interval progressively lengthens out to $\frac{3}{4}$ sec.. Two periods of 2 : 1 block succeed.

In the first part of the tracing the pulse is regular and 60 per minute; the $a-c$ interval is normal. The regular rhythm is succeeded by a run of four quicker beats with a slight but gradual increase in the $a-c$ interval; two periods of 2 : 1 heart-block succeed.

On the 7th day, after 840 minims of tincture of squill had been taken, a

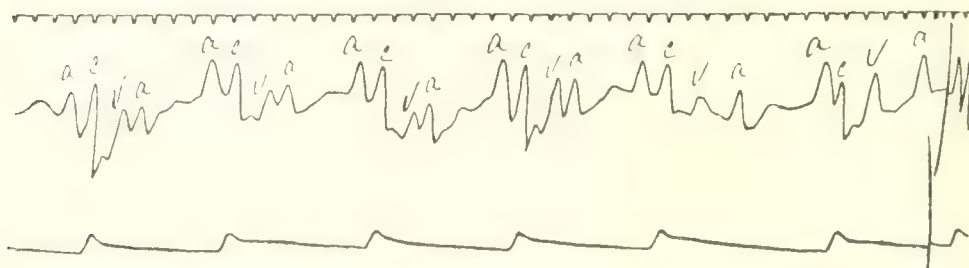


Fig. 12. Taken on the seventh day, after 840 minims squill. Shows 2 : 1 heart-block. Compare Fig. 4.

condition of 2 : 1 heart-block was present (Fig. 12) over long runs of tracing (compare this figure with Fig. 4).

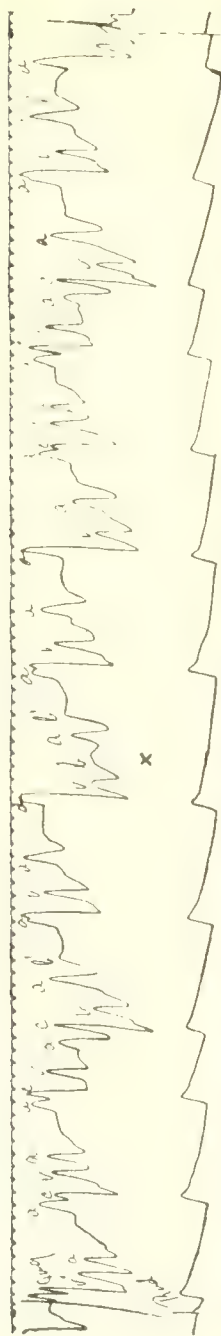


Fig. 13. Obtained after 20 drachms of the tincture of squill had been taken. From left to right two periods of 2 : 1 heart block are shown, succeeded by one period of 1 : 1 rhythm. The five following radial pulses represent idioventricular contractions, complete dissociation being present. There are nine auricular contractions to four of the ventricle. A period of 2 : 1 and 1 : 1 rhythm succeeds, after which dissociation again supervenes.

The patient was not seen again until the 10th day, when, after approximately 20 drachms of the tincture had been taken, nausea ensued for the first time but without vomiting. The general condition was very satisfactory, breathing was easy, no dropsy was present and she expressed herself as feeling very well. She felt no distress about the heart and was quite unconscious of the irregularity which is shown in Fig. 13.

This tracing is of exceptional interest, since it shows dissociation of auricular and ventricular rhythms. From left to right in the figure there are first two periods of 2:1 heart-block, the succeeding auricular impulse gets through; the four following radial pulses represent idio-ventricular contractions; complete dissociation is present during this period; there are nine auricular contractions to four of the ventricle; the independence of rhythm is obvious, *a* falls at various times in relation to *c*, and where *a* and *c* fall together the resultant wave is more pronounced; this is brought about by the simultaneous contraction of auricle and ventricle; the rate of the ventricle is 34 per minute, that of the auricle 72. Succeeding this period of complete dissociation a 2:1 block starts at the ninth radial beat, the next auricular impulse gets through and complete dissociation then appears once more.

The grades of heart-block illustrated in this figure recurred with notable regularity over long tracings. No constant relationship between their sequence and the respiratory movements was evident; the 1:1 rhythm, however, fell during inspiration with a sufficient frequency to suggest some relationship. Other waves are present in the tracing in addition to the usual *a*, *c* and *v* waves; these are marked *b* and *b'*, the latter occurs between successive auricular systoles.

A wave occupying this position in cases of heart block has been described by Gibson and Ritchie,¹ and also by Wenckebach.² The latter observers believe this wave to be the expression of the rise in pressure of the jugular vein induced by the rhythmical contraction of the muscular fibres of the superior vena cava.

There is another possible explanation which seems more probable, in this case at least.

At *x*, in the middle of the tracing, a wave *b* will be seen immediately succeeding the *v* wave; there can be little doubt from its position that this is the *b* wave described by Hirschfelder and Gibson of Oxford, and attributed to diastolic closure of the auriculo-ventricular valves. I think the wave *b'* bears the same explanation. This view is supported by the fact that on auscultation a well marked third sound was heard, coinciding, so far as could be estimated, with the rise in the tracing marked *b'*. Both the sound and the wave are explicable on the assumption that the inrush of blood from the contraction of the auricles opens the auriculo-ventricular valves and that they at once come into apposition again as the result of back flow from ventricular distention.

In another communication I have illustrated the occurrence of this wave in other cases after the administration of digitalis.

The effects of apocynum.

On December the 6th, 1910, symptoms of heart failure were again in evidence, the pulse was quite regular at 100 per minute. The patient was extremely breathless on the least exertion, and the feet and legs were swollen. Extract of apocynum in doses of $\frac{1}{2}$ grain was given three times a day* and the patient was kept in bed. The drug had no noticeable effect on the pulse until the ninth day, when the rate was 75 per minute. The tracings are not reproduced since they present no features of interest; the conduction of impulses was not impaired. On this day somewhat severe vomiting and diarrhœa ensued and the drug was omitted.

DIGITALIS.	STROPHANTHUS.	SQUILL.	APOCYNUM.
15 minims three times a day.	15 minims four times a day.	30 minims four times a day.	$\frac{1}{2}$ grain three times a day for nine days.
First effect on conductivity noticed on the 12th day, after 540 minims.	First effect on conductivity on the 9th day after 540 minims.	First effect on conductivity on the 7th day, after 740 minims had been taken. Long runs of 2:1 heart-block.	Vomiting and diarrhœa. No effect on conductivity. Pulse slowed from 95-75.
13th day coupled rhythm.	Alternate bigeminy; two days later 2:1 heart-block.	On 10th day, after 20 drachms, complete dissociation.	
14th day, after 10 $\frac{1}{2}$ drachms, alternate 1:1 and 2:1 rhythm. Vomiting.	Nausea.	Nausea, but no vomiting.	
	13th day, after 12 drachms strophanthus had been taken, severe vomiting, 2:1 and 3:1 rhythms.		

SUMMARY.

(1). A case of rheumatic mitral disease is described in which various degrees of heart-block resulted from the administration of digitalis, strophanthus and squill, respectively, during attacks of heart failure with dropsy. Marked improvement in the patient's condition was manifest under the full influence of each drug. The administration of apocynum had no effect on the conduction of impulses.

(2). A notable feature in the records, taken before these drugs were given and after their effects had passed off, was the absence of impaired conductivity as evidenced by the duration of the intersystolic interval.

* The extract was prepared in tablet form for me by Messrs. Willows, Francis, Butler & Co.

(3). It has generally been thought that drugs of the digitalis group as a rule only depress conductivity, when this function is primarily impaired, as evidenced by a lengthened *a-c* interval. The present case suggests that an actual or potential impairment of conductivity may exist with a normal intersystolic period: the facts of another case incidentally referred to lend support to this view.

(4). In some of the records, absence of ventricular response to the corresponding auricular impulse is shown, though the stimulus is apparently conducted at the normal rate in the beats immediately preceding.

(5). In some of the figures an extra wave, *b'*, succeeds the blocked auricular impulse; this wave is ascribed to the opening of the auriculo-ventricular valves by the contraction of the auricle, and their subsequent closure from back flow of the intruding blood.

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PULSUS IRREGULARIS PERPETUUS WITH FIBROSIS OF THE SINUS NODE.

BY G. DRAPER.

(*Rockefeller Institute, New York*).

THE sinus node of Keith and Flack⁶ is now generally accepted as an anatomical entity. There is also convincing evidence that it is in this structure that the heart beat arises.[†] The effects of pathological changes in the node are not yet definitely established, however, and for that reason, the present case of *pulsus irregularis perpetuus*, in which fibrosis of the node was present, is reported.

Dehio,² and more especially his pupil Radasewsky,¹³ Henchen⁴ and Koch⁷ have shown that extensive fibrotic changes in the right auricle are very often found in hearts that have been arrhythmic. Recently, Koch has reported a small series of cases, clinically diagnosed "*pulsus irregularis perpetuus*," whose hearts showed advanced fibrotic changes of the right auricle, especially dense in the sinus node; but later, Hedinger³ and his pupil, Schönberg,¹¹ published separately a series of cases of perpetual arrhythmia and described the most advanced changes in the so-called bundle of Wenckebach. Though each school of observers tends to favour its particular findings, it is only fair to say that each considers the general disease of the right auricle as the pathological factor essential to the clinical picture.

The present case belongs in the group described by Koch, for the most intense changes are in and about Keith's node. The patient, a man of sixty years, first sought treatment in the Pennsylvania Hospital for his present complaint of dyspnœa two years ago. Forty years before, he had had pneumonia and ten years later a long course of rheumatism. Since his early manhood, he had smoked fifteen cigars and drunk about a pint of whisky daily. His denial of syphilis was subsequently strengthened by a negative Wassermann reaction.

Physical examination: Patient in great dyspnœa, with rapid, grunting expirations. There is noticeable exophthalmos. The venules over the face and nose are dilated; this condition also exists along the attachment of the diaphragm. The heart is enlarged to the left, but the border cannot

From the Ayer Clinical Laboratory of the Pennsylvania Hospital, Philadelphia.

Leger has shown that destruction of the region of Keith and Flack's node causes no change in auricular rhythm, but this work has not been confirmed. Th. Lewis,⁹ on the other hand, by galvanometric curves, clearly shows that region to be the pace maker of the heart. Recent work of Lewis and Oppenheimer¹⁰ confirms this, as also does the report of Cohn and Kessel.¹

be definitely determined, owing to the adjacent flatness of note in the left axilla and posterior left chest. The apex sounds are best heard in the sixth left interspace 13 cm. from the mid-line. Here, there is no definite murmur, but in the second right space there is a soft, systolic bruit. The aortic second sound is clear and ringing. The pulse is eighty-eight per minute and described as of "poor tension and volume"; but the blood pressure is recorded "Systolic 170; Diastolic 120 mm. Hg.". On the day before discharge (five weeks after admission) there is a note that the heart is irregular.

Re-admission. The patient returned to the Pennsylvania hospital after ten months, with dyspnœa, dizziness in the morning and noises in his head. For the past two weeks, the constant tinnitus was relieved only by bending forward. Urine scanty for two days past. Physical examination reveals a patient with florid complexion, slightly jaundiced and with lips cyanotic. Exophthalmos is marked. The blood vessels are sclerotic and the veins of the neck are prominent and pulsate. The right border of the heart is 2.5 cm. to the right of the sternal edge; the left lies in the sixth space 10 cm. to the left of the mid-line. No impulse is visible or palpable. The heart sounds are very irregular, weak, slow and often bigeminal* in character. At the mitral and tricuspid areas there are harsh, blowing, explosive, systolic murmurs. There is no thrill. All the heart beats reach the wrist. The feet are cold; the tips of the toes are bluish. No pulse is felt in the dorsalis pedis or tibials of either foot. The feet are painful and tender.

Note three days after admission: The sounds at the apex are in couples. The second beat of the pair is more feeble than the first and seldom sends the pulse wave further than the carotid artery. This couplet of beats is followed by a pause of varying length and then by another pair, or less frequently, by a very weak, poorly defined, single beat which does not reach the wrist.

Note nine days after admission and the day before death. The bigeminal rhythm is no longer present, but there is now an irregular arrhythmia in which every beat reaches the wrist.

Tracings taken from the case on three different occasions show in general the same characteristics. Those from the date of April the 21st, 1910, three days after admission, indicate the bigeminal action described in the clinical notes. The last set of tracings, made six days before the patient's death, are very similar to the first set, dated April the 19th, 1910 (Fig. 1 and 2). No later ones were made. At no time could a tracing from the apex impulse be obtained.

Except for the examples of bigeminal action, which represent relatively short periods of time, the heart was constantly irregular. The jugular curve

* The term bigeminal is used here not in Wenckebach's restricted sense, but in the one suggested by Lewis. Unfortunately, electrocardiograms could not be obtained, so that the point of origin of the second beat could not be absolutely determined.

shows practically the pure ventricular type, except that the very large *v* wave is separated from the *c* wave by a notch of varying depth. Such curves resemble in considerable detail those published by Mackenzie,¹² from the cases termed by him "nodal bradycardia". Very long and large diastolic filling waves occur in almost every tracing. The *a* wave is not definitely present in any of the curves. In Fig. 1, it is possible that the wave so marked really represents co-ordinate auricular contraction; but in all the tracings from the case, this is the only instance of the sort. On the other hand, in the long diastolic pause preceding the fifth wave in Fig. 1, faint undulations, suggesting fibrillation of the auricle, appear. The number of the ventricular contractions per minute was calculated from several strips of tracing and showed during the bigeminal rhythm the following rates: 55, 45.2, 63.4. When a single rhythm existed, the rates were lower: 39.6, 50.9, 33.3 and 36.1.

In this present case, the auricles may be assumed to be in a state of fibrillation because of the complete character of the arrhythmia and the form of the venous pulse. As will be seen later from the description of the sections from the case here reported, disease of part of the conducting apparatus existed.

Post-mortem.

The patient came to autopsy, and the following notes are taken from the post-mortem record. Anatomical diagnosis. Mitral and aortic endocarditis (aortic stenosis and insufficiency); advanced parietal endocarditis with calcification; endarteritis deformans of aorta and coronary arteries; chronic cardiac hypertrophy and dilatation; fatty degeneration of the heart; acute fibrinous pericarditis; chronic fibrous pericarditis; pulmonary oedema; chronic pulmonary emphysema; chronic passive congestion of all viscera; chronic interstitial nephritis; infarction of spleen. A detailed description of the other viscera is omitted, because all showed the usual changes found in chronic heart disease. The description of the heart, however, follows. The parietal pericardium is found to be adherent everywhere to the surface of the heart by rather soft fibrinous adhesions, which being separated leave shaggy surfaces. A small amount of bloody fluid exudes in the separation. The heart weighs 700 grammes. The epicardium is covered almost everywhere by a rough beard-like fibrinous exudate. In some places also, there are milk-white patches. The epicardial fat is increased in amount. On the right side of the heart the cavities are found to be dilated. There is a thrombus in the tip of the right auricular appendage. The endocardium is smooth and glistening, here and there showing some whitish thickenings and the heart muscle shining through is rather yellowish brown in colour. The foramen ovale is closed. The tricuspid valves have only lost their delicacy to a slight degree. The pulmonic valves show a similar condition. The pulmonic artery presents a few

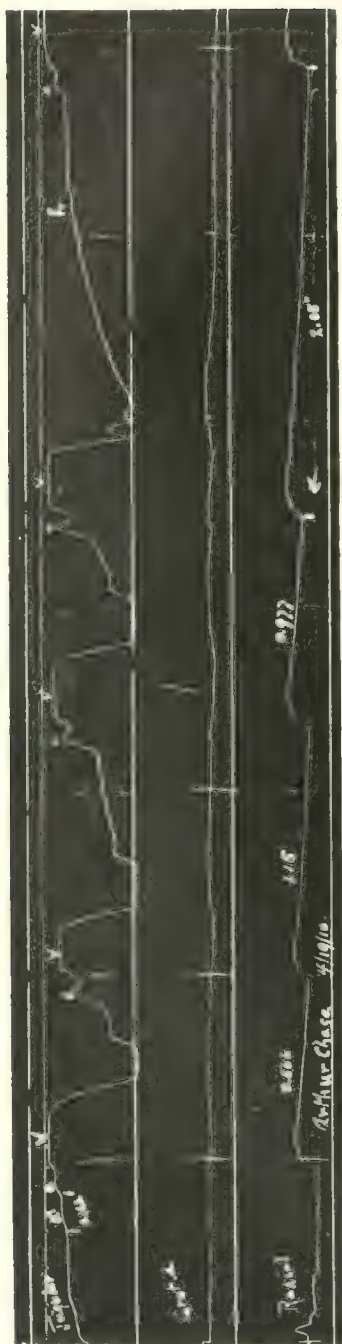


FIG. 1.

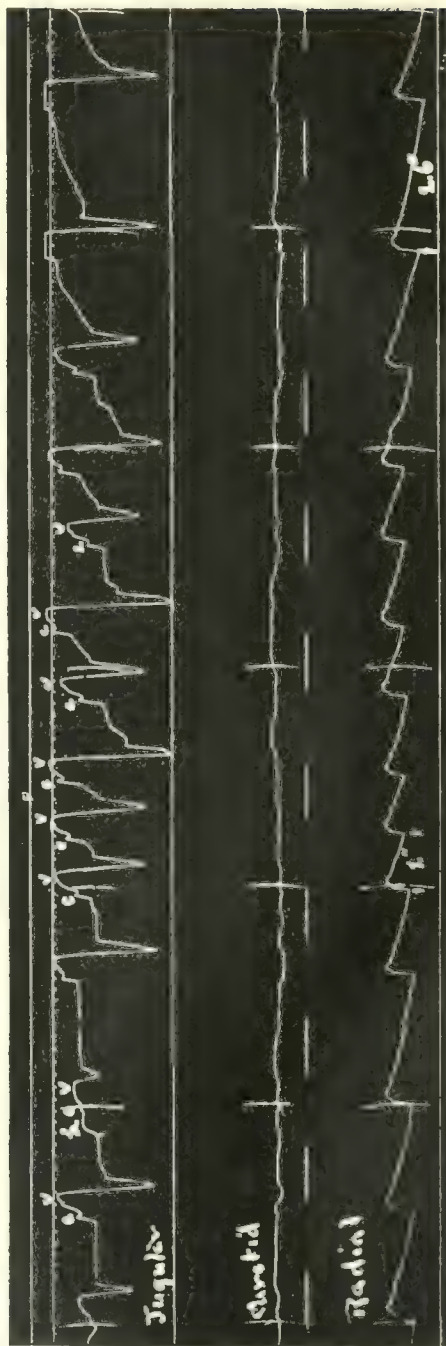


FIG. 2.

small yellowish flecks. On opening the left side of the heart, the endocardium is again smooth and glistening, except at the base of the aortic leaflet of the mitral valve where there is a dense yellowish thickening that extends outward beneath the aortic valves toward the undefended space. The endocardium below this, in the region of the bundle of His, shows rather grayish thickening. This condition increases as the apex of the cavity is approached, where the endocardium takes on a very thick tough yellow appearance and in the extreme tip has definite calcareous deposits. The mitral valve is somewhat thickened in a diffuse way and along its margin are numerous small subacute vegetations. The aortic valve is very much thickened and the cusps are fused at their angles for several millimeters. The margins of their attachments are much thickened and apparently contain some lime deposits. The coronary arteries are much diseased, presenting great thickening and yellowish patches and frequent depositions of lime salts. The base of the aorta is also the seat of many patches of yellowish thickening, which often contain lime salts. The descending aorta is somewhat dilated. The muscle, though very thick, is distinctly soft in consistency, and on section presents many yellowish fleckings. The aorta is extensively diseased throughout its entire length, presenting a series of irregular, yellowish thickenings and ulcers, many of which contain calcium salts.

For microscopical study, blocks of tissue were taken from various portions of the heart as follows :—

- I. Wall of left ventricle (left outer).
- II. Thickened endocardium and subjacent muscle of ventricular septum (left side).
- III. Papillary muscle (left ventricle) and *chordæ tendineæ*.
- IV. Auriculo-ventricular junction.
- V. Three parts of right auricle, one of which was from the region of the so-called Wenckebach bundle.
- VI. Junction of superior vena cava and right auricle.

I.—Wall of left ventricle. One margin of the section presents a layer of young connective and fat tissue, surmounted by an irregular mass of fibrin, showing organization in places. The other margin (endocardium) shows a wide strip of most extensive fibrous change. Indeed the great dense masses of fibrous tissue cover more space than the muscle bundles. This fibrous tissue contains few cells and looks old. The muscle fibres show the cross striations fairly well.

II.—Endocardium of ventricular septum and subjacent muscle. Sections show great thickening of the endocardium and strands of connective tissue

extending into the muscle. The section was taken so as to include a portion of the left limb of the auriculo-ventricular bundle. No fibres belonging to that structure could be identified.

III.—Papillary muscle. Sections show junctions of one of the *chorda tendinea* with the anterior papillary muscle. Fibrous changes and granular appearance of large areas of muscle fibres occur at this point.

IV.—Auriculo-ventricular ring. The block was taken from the upper part of the inter-ventricular septum in such a way that its upper border ran from just below the mouth of the coronary vein, and passed forward and slightly downward across the lower part of the undefended space for a distance of 2.5 to 3 cm.. The lower border of the block was parallel to this at a distance of 1 cm.. The ends of these cuts were joined. Serial sections were made from the long upper border through the whole block. Two short ribbons, five sections each in series, were mounted and then a long ribbon of ten sections left dry and unmounted. Then two more slides of five sections were mounted and so on. One slide of each pair was stained by hæmatoxylin-eosin and the other by Mallory's connective tissue stain. The plane of the section was such that the auriculo-ventricular bundle could be clearly followed in longitudinal section from the node to the point of division. From this point onwards the two limbs appeared in cross section. Examination of the stained sections showed certain places where it seemed necessary to look at the unmounted sections lying between and in these cases the appropriate dry ribbons were mounted and stained. Altogether about five hundred sections were examined. They showed in general that the muscle fibres of the bundle were fairly well preserved throughout. In no place was there a definite break of their continuity, but scattered through the whole length of the structure were patches of fibrous tissue, with here and there collections of small round cells. In the fibrous septum larger collections of these cells appeared, but the bundle in its passage through the septum showed only a few scattered lymphoid cells and some slight extravasation of erythrocytes. The A-V node also demonstrated a few scattered small round cells and possibly a slight increase of connective tissue. Of course, it is impossible to say to what extent these scattered changes affected the functional power of the bundle, but despite the presence of the fibrous patches and the small round cell infiltration, there seemed still to be a large amount of muscle fibre present.

V.—Auricular wall. Sections from three different regions of the right auricle all showed some fibrous changes, but not very marked ones. Pericardial thickening, however, with small round-cell infiltration and young connective tissue cells in profusion, was marked. Indeed this pericardial change was the most striking feature of the pathological anatomy of the auricular wall.

VI.—Junction of superior vena cava and auricle. The block was cut so that the sino-auricular groove lay equidistant from and parallel to the two

long margins, the upper margin lying in the superior vena cava and the lower in the auricle. The anterior ends (heart held with the left ventricle as its long axis) of these margins were joined by a cut which passed through the angle of the junction of the right auricular appendage and the superior vena cava. The posterior ends were joined by a cut parallel to the anterior and about 3 cm. distant from it. Serial sections, whose plane was at right angles to the long axis of the block, were made of the whole piece. The same system of mounting and staining described above was used. In all about fourteen hundred sections were examined. The sinus node of Keith and Flack is well shown in its whole length and presents a high degree of fibrosis. The pericardium, overlying the junction of the superior vena cava and auricle, is thickened and infiltrated with numerous small round cells. Groups of these are seen just beneath the dense pericardium immediately next to the sinus node. A little below the level of the middle of the node there is a definite nodular thickening of the pericardium. Many young fibroblasts appear and several small blood vessels containing masses of lymphocytes and red blood cells. Occasional large ganglion cells and a few tortuous nerves appear. The endocardium also shows thickening, but very few infiltrating cells are seen. Between the auricular muscle fibres there is marked increase of the connective tissue strands, and these often fuse to form small dense islands of fibrous tissue, containing very few cells. The node presents less complete fibrosis at its two ends than in the central portions. Near the poles a few small, poorly staining muscle fibres still appear among the interlacing fibrils of connective tissue, but the central portion of the structure is completely fibrous. The constant artery shows no marked pathological changes. In the sections from the lower part of the node a small vessel is seen containing an organized canalized thrombus.

It will be seen from the description of the microscopical preparations that by far the most extensive fibrous change exists in the node of Keith and Flack. The pericardial disease is also strikingly intense over the region of the node. In regard to the rest of the auricular wall, it can be fairly said that signs of chronic inflammation are universally distributed; and sections from the lower part of the auricle in the region of the inferior vena cava and so-called Wenckebach's bundle show no greater involvement than any other part.

Furthermore, it is a striking feature that the auriculo-ventricular node and the main trunk of the auriculo-ventricular bundle are but slightly affected. This portion of the conducting mechanism is apparently in a condition to functionate, but in view of the extreme thickening of the parietal endocardium along the septum and apex of the ventricular cavity and about the bases of the papillary muscles, one is led to suspect the destruction of much of the terminal ramifications of the bundle.

The lesions in this case are strikingly similar to one reported by Krumbhaar,⁶ which showed the typical Adams-Stokes syndrome with

auriculo-ventricular dissociation and regular ventricular rhythm. In the sections of that case, which the present author has had an opportunity to study, fibrosis of the sinus node was found, but there was insufficient lesion of the auriculo-ventricular bundle to account for the block. Here then, are two cases which strengthen the belief that perpetual ventricular arrhythmia occurs when the auricle is in fibrillation, provided the auriculo-ventricular conducting apparatus is not absolutely demolished; but upon the proposition that destruction of the sinus node is the etiological basis of *pulsus irregularis perpetuus*, they afford divided evidence. Krumbhaar's case showed fibrosis of the node, but the auricle was not fibrillating, for there were well marked *a* waves in the jugular tracings. Auriculo-ventricular dissociation existed, but there was no lesion of the auriculo-ventricular bundle and the ventricular action was regular.

The case here reported presents, in contrast to Krumbhaar's, a fibrotic node beneath which a fibrillating auricle may with good reason be suspected. Perpetual arrhythmia of the ventricles and the absence of the *a* wave from the jugular tracings are almost adequate proof of this condition. The slow rate, which at times gives a semblance of regularity of rhythm, suggests perhaps a partial block of the auriculo-ventricular bundle, and this view is strengthened by the anatomical findings.

When these facts are considered from the anatomical standpoint, in connection with the other cases in the literature, one is left as much as ever in doubt concerning the etiological specificity of the sinus node lesion. It adds one more case to Koch's series certainly; but Krumbhaar's example stands in strange contradiction. As a physiological consideration, however, it undoubtedly furnishes, with the two cases discussed, further evidence of the close relationship between auricular fibrillation, diminished functional power of the conducting paths and the slow form of *pulsus irregularis perpetuus*.

My thanks are due to Dr. J. C. Wilson for permission to use the clinical notes of the case, and to Mr. W. B. O. Field for the great interest which he took in making the photomicrographs of the sinus node.

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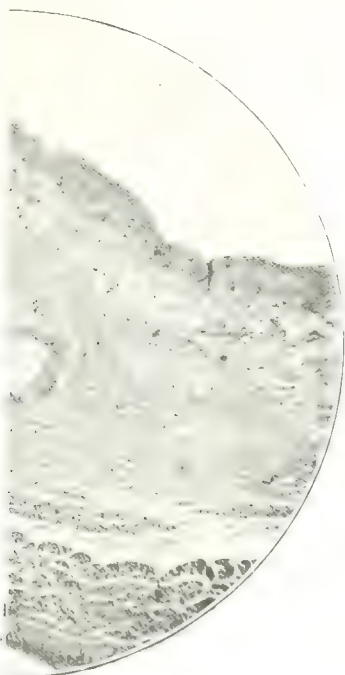
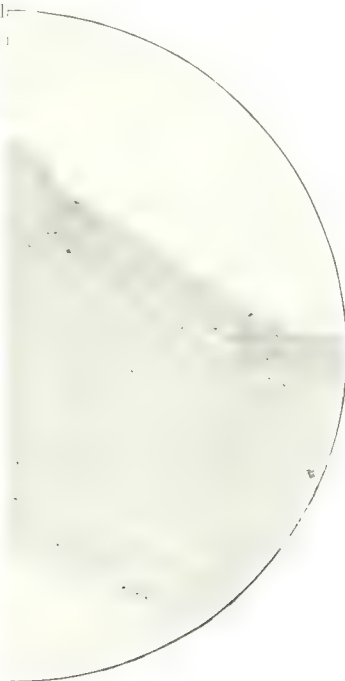


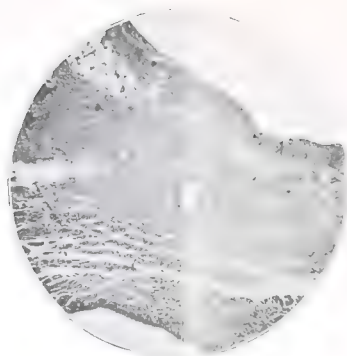
Fig. 3. Node of Keith and Flinn
location about 53 diameters
pericardium

3

Fig. 4. Node of Keith and Flinn
54 diameters. Showing 1



4.



A CASE OF BRADYCARDIA WITH POST-MORTEM EXAMINATION.

By ALFRED E. COHN.

(*New York*).

IN the first number of this *Journal*, Dr. James Mackenzie published a group of cases which he termed instances of "Nodal Bradycardia." *CASE 3*, reported at that time, has since died, and a post-mortem examination has been made. Dr. Mackenzie kindly entrusted the heart to the present writer for histological examination, and these findings are now to be reported, together with a somewhat fuller account of the clinical history.

The patient, W. N., a male, was born in 1838. Dr. Mackenzie had occasion to examine him in 1906 and found him in normal health and his heart normal in rate and rhythm, except for an occasional extra-systole. His habits had been good except that for a great many years he had "smoked two ounces of tobacco and half a dozen cigars a day." In February, 1907, for some unexplained reason, his heart action became continuously irregular. He had been short of breath, but beyond an increased severity of this symptom he had not been aware of any change. Later in 1907 he suffered attacks of unconsciousness, which kept recurring for a while; during them his pulse rate dropped to thirty a minute. In November of this same year, the fainting attacks returned, but he was too weak to allow tracings to be made; his pulse rate was again thirty. By June, 1908, he had recovered somewhat; his pulse rate had returned to sixty and he went to Torquay. He continued quite well until August the 4th, 1908, when during physical strain, he was seized with great breathlessness. Then for two days he began to have convulsive seizures every few minutes for a couple of hours, from which he was ultimately relieved by chloroform. During the attacks his pulse could not be felt and he became cyanosed. The attacks frequently came at night. They continued for a month, gradually becoming less in number and slighter in severity, appearing finally as nothing more than a passing faintness. During this period he was under treatment by Dr. O'Connor, who described some of his attacks as resembling "petit mal"; he says that while talking his face would become pale, unconsciousness would set in for a brief interval and his pulse would always disappear. In other attacks he was quite unconscious, sometimes delirious, and would struggle to get out of bed. During August and September he had Cheyne-Stokes breathing, respiration being suspended for as long as forty-five seconds. In September, 1908, his pulse rate rose to sixty, while in October he had a large number of fainting attacks, which subsequently disappeared, but left him weak. Cognac is said to have relieved him.

On December the 18th, 1908, tracings were taken, which demonstrated the presence of irregularity accompanied by the ventricular form of venous pulse. Some of the heart beats were so weak that they were scarcely felt at the wrist. At this time, the heart dulness (left border) extended one and a half inches beyond the nipple line; there was faint roughening of the first sound, but there were no murmurs. Slight albuminuria, which increased somewhat during his illness, had been present for some years; there was no dropsy. At this time, however, there was no albuminuria, but he micturated frequently.

On March the 10th, 1909, Dr. O'Connor reported that the patient had been well since Christmas, that he went to town to business and looked well,—in short, that he had recovered. During the first week of March he had a few slight fainting attacks, said to be due to over eating. His pulse rate was sixty and fairly regular. His urine contained no albumin. He had given up smoking for four months past, and during his attacks or when he felt ill, he took trinitrin gr. $\frac{1}{100}$; oxygen and amyl nitrate also seemed to do him good. On May the 7th, 1909, Dr. O'Connor mentions the presence of a soft blowing systolic murmur with the first sound, heard four inches to the left of the median line and on a level with the nipple. The liver was much enlarged. His pulse was sixty and fairly regular. He felt well and went to town regularly on business. He was of the opinion that smoke brought on an attack. In June he fell unconscious and fractured the lower end of one fibula, but after six weeks rest, he made a good recovery, went to town and played golf daily. On August the 12th, 1909, he died suddenly, after having had a chill from sitting out and contracting pneumonia. Although the pneumonia cleared up, his heart was left weak; the pulse beat at a rate of twenty-five and was thready in character. He had anuria for one day and a single convulsion. On the evening of the day before, his pulse had been imperceptible, he was given strychnine, gr. $\frac{1}{10}$, and it rose to forty, but while taking food next morning, he died suddenly.

Dr. O'Connor performed a hasty autopsy, the notes of which are given here. The *heart* was enlarged and there was a cartilaginous deposit about the valves. The capsules of the *kidneys* were adherent; they were enlarged and looked cirrhotic. There was great increase of pelvic fat. The *liver* was larger than normal but looked healthy on section. There were old adhesions on the surface of the right lung, together with recent signs of pneumonia and pleurisy.

Specimens of the tracings taken on October the 11th, 1907, are shown in this *Journal*, Vol. I, p. 31, Fig. 9 and 10. These show a pulse rate of twenty-five to thirty beats a minute, and indicate the presence of the ventricular form of venous pulse. In some of the longer reaches, where there is no indication of a contraction in the radial curve, there is a premature wave in the jugular tracing, similar to, but not identical with, the preceding sequence. The tracing taken on May the 5th, 1909, shows also the presence of the ventricular venous pulse, but the rate is about eighty-three per minute. Thus there were

periods when the rate was rapid, others when it was slow. The tracings always showed a disordered rhythm, though even late in the disease Dr. O'Connor reports that there were times when the pulse was "fairly regular." In another case (*CASE 1*) belonging to this group, Mackenzie states that the bradycardia was not constant, but that the heart returned from an irregular bradycardia to a regular rhythm and a normal rate, and furthermore that the change occurred without any subjective symptom. It is clear, therefore, that as in the case of the corresponding fast irregularity, a return to a regular rhythm can and does take place.

Esmein¹ refers to Mackenzie's cases and himself reports three others. In one case he first noted a period of incomplete heart-block, with syncopal attacks, later the patient developed complete heart-block in which the administration of atropine quickened the auricular but not the ventricular rate. A few months afterwards, the auricular waves disappeared and the ventricular form of venous pulse was present. His second and third cases showed bradycardia accompanied by the ventricular form of venous pulse. Autopsies were made in the first two patients and showed an old lesion of the A-V bundle. Esmein does not admit Mackenzie's theory that the rhythm in these cases begins in the A-V node, chiefly because he cannot conceive how the node can give rise to so slow a rate. If the node has undergone a change at all it ought, in his view, to be the site of an irritative lesion, which would render it more readily excitable than the sino-auricular node. But since increased rate is not the fact in these cases, Esmein is inclined to rely on a paralysis of the auricles by distension, as an explanation of the phenomenon. Esmein's communication itself is not available here so that an account of the tracings and of the histology of his cases cannot be reviewed.

A similar case of bradycardia is mentioned by Mackenzie (*CASE 4*) in his original paper and was described later in detail by Lewis.⁴ As in the case here reported, Lewis's case had a pulse rate from twenty-seven to thirty-five a minute, and showed the ventricular form of venous pulse, but the rhythm was *regular* except where it was interrupted by extra beats. Furthermore syncopal and epileptic attacks occurred as in the case at present recorded. The essential difference between Lewis's patient and the case now reported resides in the fact that here there is no regularity in the heart rhythm, though the similarity in other respects is striking. Lewis described his case as one of auricular fibrillation and heart-block and was justified in the diagnosis by the electrical curves. There is, however, as yet, no anatomical verification of his assumption of heart-block. In the present instance, as will be described later, this analysis of the mechanism is not supported by the anatomical findings.

Anatomical examination of hearts from patients showing irregularity and the ventricular form of venous pulse with rapid heart rate (*pulsus irregularis perpetuus*) has been undertaken and described by Keith and Mackenzie,⁵ Koch,³ Schönberg⁶ and Hedinger.²

In the hearts supplied to him by Mackenzie, Keith⁵ described changes such as the assumption by the fibres of the *A-V* bundle of the characteristics of the normal heart muscle, stretching of the fibres of the bundle, flattening of the *A-V* node; atheroma of the artery to the *A-V* node. In the muscle of the ventricle itself he found extensive fibrosis and rheumatic nodules. In another case he found the fibres of the *A-V* bundle fibrosed and atrophied. In still another he found the sino-auricular node sclerosed, together with other minor lesions of the *A-V* system. Hypertrophy of the *tunica terminalis* was a frequent finding. CASE 12 showed closure of the anterior interseptal artery. Although no single pathological lesion responsible for the disordered rhythm is assigned, it seems clear that Keith laid more emphasis on changes in the auriculo-ventricular system than in the supraventricular portions. This emphasis was the more natural at a time when the explanation of the occurrence of the arrhythmia was ascribed to the *A-V* node. Koch³ examined three hearts, two of Hering's and one of Delacamp's. Briefly, investigation yielded no anatomical lesion which he was inclined to regard as the ultimate cause of the clinical findings. Although the three cases showed slight differences, they revealed similar changes. Two showed hypertrophy of the right auricular muscle, especially that of the *tunica terminalis*; there were collections of round cells, some fatty degeneration of the muscle, but the vessels were intact. The sino-auricular node was atrophic, and showed sclerotic changes and some fatty infiltrations. The nerves and ganglia also contained some round cells in their sheaths. The nutrient vessel was quite normal in his cases. The auriculo-ventricular node except for some unimportant changes, as well as the rest of the auriculo-ventricular system, showed no abnormality. These investigations, in short, did not allow of definite conclusion.

Schönberg's⁶ papers, in which he lays stress on the occurrence of lymphocytic infiltrations in the region of the Wenckebach's bundle, rely for their significance on a function which is no longer attributed to that structure. Hedinger more recently describes lymphocytic infiltrations in the regions about the entrances of the *venae cavae*, but he does not regard the findings as of definite significance.

From the various views and anatomical lesions which have been put forth to account for the occurrence of a perpetually irregular pulse, it is apparent that no single lesion can as yet be regarded as the ultimate causative factor. It might indeed be doubted whether an anatomical change need be responsible in these cases, in the light of Lewis's work, and Rothberger's and Winterberg's, on auricular fibrillation. Until a decision on its causation in both the slow and rapid forms is finally reached, anatomical investigations must continue, and it is with this view that the study of the present case has been pursued.

The heart was received from Dr. O'Connor, fixed in formol-Müller solution, embedded in celloidin-paraffin, and cut in sections 10 micra thick.

Every fifth section was mounted and stained with iron hamatoxylin and Van Gieson's solution.

The heart measured 13 cm. across the base along the auriculo-ventricular groove; from the upper end of the inter-auricular septum to the apex, 16 cm.; and in thickness, again at the auriculo-ventricular groove, 8 cm.. These measurements were made subsequent to fixation. There was considerable fatty overgrowth over the anterior surface below the *A-V* groove and some behind along the furrows accompanying the vessels. There was hypertrophy of the right ventricle; at the base the muscle measured 9 mm., and 1 to 2 mm. at the apex; at the conus near the valves it measured 6 mm.. The wall of the right auricle at its right border and close to the ring measured 7 mm.. The *tunica terminalis* at its upper end was hypertrophied, measuring 16×12 mm.; its shape was roughly triangular on cross section. The muscular bands of the right auricle were distinctly hypertrophic. Fatty changes in the muscle and muscular changes in general could no longer be determined macroscopically. The tricuspid valves in the fixed state admitted three and a half fingers, measuring 3.5 cm. in diameter. They were normal and may easily have been normally competent. The pulmonary valves were quite normal except for slight fenestration of the posterior flap. There was a well developed Chiari net at the opening of the coronary sinus.

The left auricle was somewhat dilated and measured 6 cm. in transverse diameter. It showed no hypertrophy and in the recent state the endocardium must have been white. The left ventricle was not dilated; at its base the wall measured 18 mm. at the left border, and 15 mm. at the right border; at the level of the papillary muscles, 16 mm., and at the apex, 10 mm.. The posterior flap of the mitral valve was slightly thickened at the edge: on the ventricular surface there was atheroma of the aortic flap. There was likewise along the line of closure of the aortic (anterior) flap in its right half a few thread-like vegetations, which were not friable, but firm and old. The diameter of the mitral ring was 3.2 cm.. The anterior cusp of the aortic valve was slightly fenestrated; along the *lunulae* and on the *corpora Arantii* there were a few thread-like vegetations similar to those described on the mitral valve. In the sinuses of Valsalva on the cusps of the valve were some atheromatous, possibly sclerotic patches. There was slight atheroma of the aorta. The *foramen ovale* was closed.

I excised for examination:

1. The region of the sino-auricular node.
2. The auriculo-ventricular septum containing the *A-V* node, the main stem and branches.
3. A portion of the left auricle.

4. A portion of the right auricle.
5. The papillary muscle.
6. A piece of the left ventricle.

The connective tissue surrounding the vessels in the tissue from the *left ventricle* is somewhat increased: a not abnormal amount of fat is to be found here as well. Small star-shaped scars radiate between the muscle fibres, compressing them and causing atrophy: they are rather numerous. The *papillary muscle* like the rest of the ventricle shows a number of scars, somewhat larger, but not more numerous than in the latter. The *left auricle* shows an ingrowth of fatty tissue, a slight increase in interstitial connective tissue, and here and there moderately large collections of inflammatory cells, mostly lymphocytes and plasma cells, but also some leucocytes. In the *right auricle* there is a marked thickening of the connective tissue which passes between the individual muscle fibres: the fibrosis is far in excess of that found under normal circumstances.

The *sino-auricular node* is a well developed structure, made of muscle fibres of a size and interlacement now well known. The fibres in this case show a well-marked fine striation. Their intimate relation to and gradual transition into auricular tissue can be well seen. Nerve fibres pass in the immediate neighbourhood of the node and an occasional one is seen to enter the structure from the pericardial side. The artery, often described, is present in this case: great changes have not taken place in it but occasionally an endarteritis, especially of smaller branches, can be made out. The increase in connective tissue within the node is most marked. Beyond an allowance for individual variation, this seems to be unusually marked, and can be followed through the node in its entire extent. Furthermore, it is out of all proportion to the amounts which are seen in the neighbouring auricular musculature. Round cells are found in moderate numbers and, in places, leucocytes are added to these. In parts also the node is oedematous. In one or two places there are small hæmorrhages, probably agonal in incidence. It will be remembered that increase in the connective tissue of the *sino-auricular node* is a change which Koch has mentioned, as a possible factor in the etiology. While it cannot be affirmed that this sclerosis is causative, it should in the present state of knowledge be brought forward as a factor of importance from the anatomical standpoint.

The upper portion of the *auriculo-ventricular node* is placed in a rather small space between the endocardium of the right auricle and the central fibrous body, so that it has the appearance of being laterally compressed. At a somewhat lower level it becomes thicker. A slight increase in the amount of connective tissue has taken place, as well as a slight deposit of fat cells, but these changes cannot be considered pathological. They occur in the

main stem as well as in the node. A moderate amount of sclerosis in the vessels (endarteritis) of the node, there being several instead of the more usual single large nutrient branch, has taken place. The only other changes that might be noted are : first, that at its origin the volume of the left branch is somewhat encroached upon by connective tissue ingrowth, so that at this level the right branch seems the larger, though lower down these relations are reversed ; and second, that farther along in the course of the right branch there is a moderate increase in connective tissue.

It will be apparent in reviewing the anatomical evidence to account for the perpetually irregular pulse that the later writings (Hedinger, Koch) differ from the earlier in that the greater emphasis was formerly laid on changes in the auriculo-ventricular system, whereas now lesions in the sino-auricular node are receiving the greater attention. Sclerosis, deposits of fat cells, fatty degeneration, endarteritis and diffuse interstitial fibrosis have all been considered. It is still too early to say whether one more than the other represents the real cause. Whether the trouble resides also in one or the other node is also a matter still open for discussion. The subject is further complicated by the fact that in the cases of the perpetually irregular pulse, the hearts which yielded slow types and those which yielded fast types of pulse rate disclose on histological examination, microscopic pictures which from all accounts differ in no sense from each other. The small changes which have taken place in the auriculo-ventricular system do not seem capable of exercising so decided an influence on the ventricular rate as the event shows. It follows, therefore, that even if definite supraventricular lesions could be found to account for auricular fibrillation and the perpetually irregular pulse, the factor determining ventricular rate is still indeterminate.

The present case is, then, one of bradycardia and differs from the one described by Lewis in that the ventricular rhythm is perpetually irregular, and that in its course, there occur periods both of rapid and of slow rate. The pace-making area and the conduction system have been examined and have shown profound lesions in the sino-auricular node, interstitial myocardial lesions in the auricles and ventricles, but more especially in the right auricle, with but slight changes in the auriculo-ventricular node and branches.

I am greatly indebted to Dr. James Mackenzie for the privilege of describing this case and take great pleasure in thanking him for his help and great courtesy. The microphotographs were taken by Dr. F. S. Mandlebaum, and I take pleasure in acknowledging my indebtedness to him.

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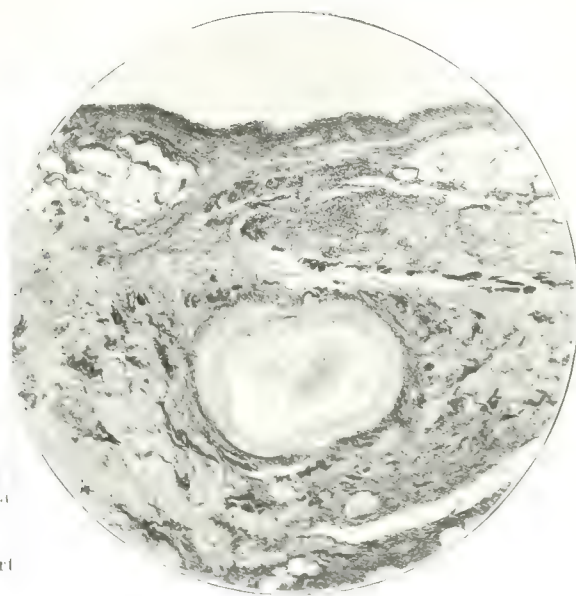


Fig. 1. The sino-auricular node from . . .
Lymphatic infiltration of subpericardium.

Fig. 2. A more highly magnified part
and the lymphatic infiltration. \times

FIG. 2

Fig. 3. The sino-auricular node from . . .
There is an increased amount of
auricular muscle and also with the

Fig. 4. The sino-auricular node from . . .
Increased amount of fat tissue is
in the amount of connective tissue.

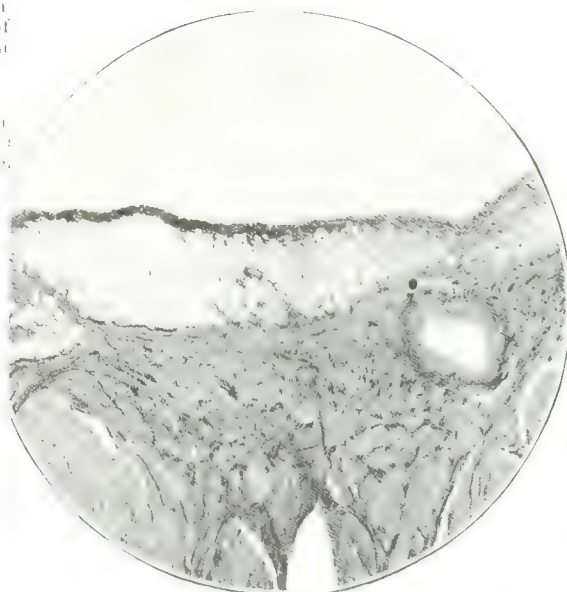


FIG. 4

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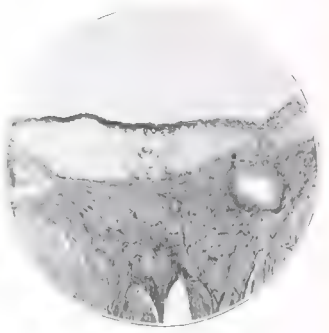
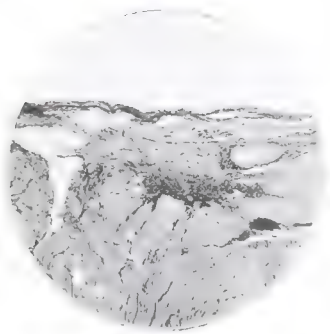
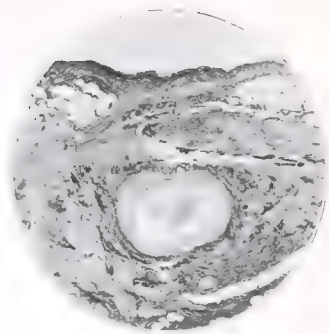
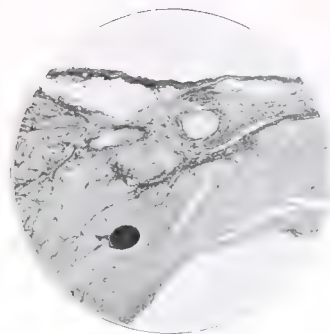


Fig. 3

Fig. 4

STUDIES ON THE CIRCULATION IN MAN.

I. THE MEASUREMENT OF THE BLOODFLOW IN THE HANDS.

BY G. N. STEWART.

(From the H. K. Cushing Laboratory of Experimental Medicine,
Western Reserve University, Cleveland).

INTRODUCTION.

FOR many clinical purposes and some physiological ones it is fully as important to know the rate of flow of the blood in a patient or the total output of the heart and the way in which they vary under different conditions as to know the arterial pressure. A modification of the method used by Grehant and Quinquaud³ in animals has been lately applied on a somewhat extensive scale to the measurement of output in man by Plesch.⁶ It may be accurate, but it is certainly neither very simple for the observer nor very easy for the patient. The method of measuring the rate of flow through the arm by means of the plethysmograph developed by Hewlett and Van Zwaluwenberg¹ from a suggestion of Brodie and Russell² appears also to be difficult, while as to accuracy, even with their fine technique they can only conclude "That the method determines the rate of peripheral blood-flow in the arm with rough accuracy, the error in favourable cases not exceeding 20 per cent.". This is not intended as a criticism of admirable work, but rather as a reason for my bringing forward another method which, whatever its limitations, is exceedingly simple, and at the same time, I think, susceptible of considerable accuracy. The apparatus and method were demonstrated, and illustrative examples of the results communicated to the American Physiological Society on December the 29th, 1910.⁷ A brief study of the hand circulation in a case of birth palsy and a case of infantile paralysis was communicated to the Society for Experimental Biology and Medicine.⁸

METHOD.

The blood flow in the hand is calculated from the formula $Q = \frac{H}{T - T'} \cdot \frac{I}{S}$, where Q is the quantity of blood flowing through the hand in the period of observation; H the heat given off to a calorimeter containing the hand, when the initial temperature of the calorimeter is made less than that of the arterial blood, or the heat withdrawn

by the hand from the calorimeter when the initial temperature of the latter is made to exceed that of arterial blood ; T , the temperature of the arterial blood coming to the hand ; T' , the temperature of the venous blood leaving the hand ; and S the specific heat of the blood. The volume of the hand included in the calorimeter is estimated by displacement, and the result reduced to grammes of blood per minute per 100 c.c. of hand substance.

1. DETERMINATION OF H . (THE HEAT GIVEN OFF BY THE BLOOD TO THE CALORIMETER).

This is done by means of the calorimeter shown in Fig. 1, which is made in duplicate for the simultaneous observation of the two hands. Where for any reason only one hand is observed, the second calorimeter serves automatically to measure the loss of heat to the surroundings. The calorimeter consists of an inner cylindrical vessel of strong, tinned copper, the tinned surface being internal, and an outer larger vessel of tinsheet, the external surface of which is painted. Between the sides and bottom of the inner vessel and the outer vessel is a layer of broken cork. The top of the inner vessel has in it an oval opening rather wider at one end than at the other for the reception of the wrist, and in use the calorimeter is so arranged with reference to the patient that the wide end of the opening faces the same way as he does. This enables the thicker part of the hand (ball of thumb, etc.), to be more easily introduced. The orifice is surrounded by a flange, upon which a thick felt collar shown above the calorimeter lid in the figure rests (Fig. 1), and which defines the upper limit of the part of the hand included in the calorimeter. The felt is a variety used by saddlers, and is $\frac{1}{2}$ -inch thick. The collars are cut so as to exactly fit each wrist. After a few patients have been examined it is, of course, rarely necessary to cut new collars. Outside the flange rises a ring of copper $\frac{1}{2}$ -inch high, which allows the top of the inner vessel to be covered with cork. Three smaller orifices, one for a thermometer and the other two for stirrers, pierce the lid, each surrounded by copper rings of the same height. Over the lid is a circular sheet of cork, $\frac{3}{4}$ -inch thick, accurately adapted to the orifices and fastened and covered with a layer of shellac. The cork packing is necessary to reduce the loss of heat, otherwise the calorimeter could not be used in places of varying temperature. In any case the temperature changes in it, due to cooling, would take place so quickly that the hand would not have time to follow them. It was only necessary to have the inside vessel made in the laboratory. A very suitable outer vessel was obtained in a store in the shape of a receptacle used by housewives and labelled "sugar". The outer vessel is $10\frac{1}{2}$ inches deep and 9 inches in internal diameter. The inner vessel is 8 inches deep below the flange and its internal diameter is 6 inches. The average breadth of the flange is half an inch. The orifice for the hand measures $3\frac{1}{2}$ by $2\frac{3}{4}$ inches. The solid cork on the lid is $\frac{3}{4}$ inch thick.

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2. Photograph
In an actual ex



Fig. 2.

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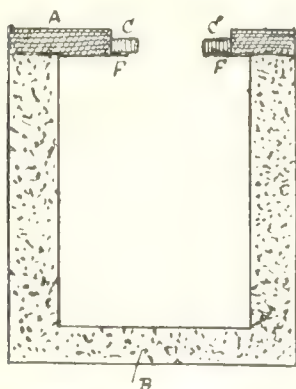


Fig. 3. Section of calorimeter, $\frac{1}{2}$ of actual size. A, sheet cork; B, broken cork; C, felt collar; F, flange around orifice for hand. The orifice is supposed to be cut along its smallest diameter.

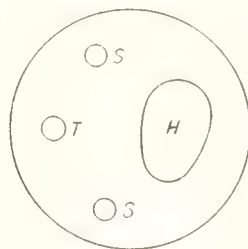


Fig. 4.—Diagram of top of calorimeter for left hand as viewed from above. H, orifice for hand; T, orifice for thermometer; S, for stirrers.

The stand on which the calorimeter rests, gripped by brass angles to prevent accidents, is provided with a long screw, which enables the height to be adjusted either to the patient sitting in a high chair or to a patient sitting up in bed. In the lowest position the top of the stand is $16\frac{1}{2}$ inches, and in the highest 27 inches, from the floor. A nut on the screw clamps it in any given position.

The thermometer is graduated in tenths of a degree, permitting the hundredths to be estimated by means of the lens shown on the thermometer stem. All thermometers used were compared with a standard certified thermometer.

Large goose feathers were used for stirring, to avoid possible injury to the thermometers.

Fig. 3 shows the calorimeter in vertical section. Fig. 4 gives a diagram of the orifices in the lid as seen from above.

In Fig. 2 is shown the position of patients who are able to sit up with the hands in the calorimeters. The coat sleeves, however, are tucked up, the better to display the orifices of the calorimeters, whereas in most of the measurements the arms were kept covered by the sleeves down or almost down to the calorimeter collars. The patient is seated in the high chair always used. The seat is $25\frac{1}{2}$ inches from the floor. The chair is high so that the observer, who most conveniently sits behind the patient on a very low seat may not have to crouch too low to read the thermometers. In the figure the patient is shown supporting his feet on one of the rungs of the chair, but during the actual observation he rests them more comfortably on another chair or a footstool. He leans back in the chair and allows his hands to hang vertically down without effort. Behind the chair is tied a thermometer which gives the room temperature.

In making an experiment the following routine is conveniently followed. Felt collars having been found or cut to fit the patient's wrists, a horizontal mark is made with an oil pencil on the back of the wrist at the lower level of the styloid process of the ulna. A parallel mark is made on the wrist proximal to this at a distance equal to the combined thickness of the collar and the flange of the calorimeter. The second mark is just to be kept in sight above the collar during the stay of the hand in the calorimeter. It is clear that then the lower mark will be just below the edge of the orifice of the calorimeter.

A large bath holding 25 litres (a new garbage can was used) is filled with water at the temperature which has been decided on for the initial temperature of the calorimeter. Generally one chooses a temperature of about 30° C. An ordinary thermometer graduated in degrees is sufficiently accurate for reading this temperature. With a little experience an assistant easily hits on the required temperature and the mixing of the bath is only a matter of a minute or two. When a patient is expected at a set hour the bath, of course, can be prepared beforehand. A large bath is used so that it may cool very little during the period of immersion of the patient's hands. The calorimeters are then filled from the bath. For hands of average size it was found advantageous to have about 3 litres of water in each calorimeter. If much more were put in, the collars were apt to be wetted during vigorous stirring, and the cooling of the wrist due to evaporation of the water was found sometimes to cause error owing to reflex vaso-constriction. If much less were put in, the air space inside the calorimeter would be so great as to lead to risk of loss of some heat through its not being all taken up by the water. Experiment I was made to test this point.

Experiment I.

1.41 p.m. put hands (et M. C.) in bath at 27.0°. Put 3,200c.c. of water in calorimeter L, 3,000c.c. in R. Room temperature 18.8°. Mouth temperature 36.8°. Pulse 107.

Time	R.	L.	
1.51 p.m.	26.75	26.59	At 1.52 put right hand into R, left into L. Subject sitting.
1.54	26.91	26.72	
1.56	27.18	27.00	
1.58	27.42	27.22	
2.00	27.66	27.47	At 2.01 removed 200c.c. of water from L without disturbing hands. The water was withdrawn by a pipette through one of the stirring holes.
2.01	27.78	27.58	
2.03	27.91	27.70	
2.05	28.09	27.87	
2.06	28.19	27.92	
2.07	28.28	28.06	
2.09	28.49	28.30	Hands withdrawn at 2.13.
2.11	28.67	28.46	
2.13	28.78	28.58	
2.23	28.60	28.40	
2.30	28.50	28.29	Room 19.2°
2.39	28.40	28.18	Volume of right hand in calorimeter 435c.c., of left 410c.c.

For the first part of the experiment (7 minutes) the flow comes out at 12.8 grammes blood per 100 c.c. of hand per minute for the right hand, 13.9 grammes for the left. For the second part (the last 7 minutes) 10.29 grammes for the right and 11.73 grammes for the left. The excess of left over right in the first part of the experiment is accordingly not conditioned by the greater amount of water in L, since it persists in the second part when the quantity of water is the same in each. In Table I the summary of results is given under M.C. 12,13.

To save time the water was measured by filling to the brim a flask holding approximately the required amount. The flask now used is made of zinc and holds 3015 c.c.. A metal funnel and jug are also used so as to relieve the observer of any anxiety about breaking glass vessels. In this way every minute is saved which can be saved without detriment, a very necessary matter in a clinical method. Jug, funnel and flask are all dipped first in the bath and then emptied before being used to fill the calorimeters so that the two calorimeters may start with approximately the same temperature. As each calorimeter is filled its orifice is closed by an exactly fitting disc of the thick felt. The patient now sits down beside the bath and immerses his hands up to the lower mark. He is directed to keep his fingers spread both in the bath and in the calorimeter so as to favour the escape of heat. The bath is stirred from time to time. Some water laps up over the lower mark but the wrist is rapidly dried with a towel before the hand is put in the calorimeter. The following experiment was intended to test the influence of spreading the fingers on the calculated blood flow.

Experiment 11.

3.28 p.m.. Hands (M.C.) put in bath at 29.0°. Room 21.1°. 3,050 c.c. in each calorimeter.

Time.	R.	L.	
3.38½ p.m..	29.07	28.87	At 3.39 put right hand in R with fingers close together but extended, and left in L with fingers spread. Subject sitting.
3.41	29.20	29.00	
3.43	29.43	29.21	
3.45	29.69	29.44	
3.47	29.89	29.63	
3.49	30.08	29.80	At 3.51½ spread fingers of right hand keeping those of left hand still spread.
3.50	30.14	29.87	
3.51	30.22	29.92	
3.53	30.36	30.01	
3.55	30.51	30.17	
3.57	30.66	30.30	Took out hands at 4.00. Room 21.2°.
3.59	30.80	30.43	
4.00	30.89	30.51	
4.09	30.79	30.41	

Volume of right hand in calorimeter 450 c.c., of left 435 c.c.. Mouth temperature 36.8°. Pulse (sitting) 96. For the ten minutes before the fingers of the right hand were spread the flow comes out 13.7 grammes per hundred c.c. per minute for the right and 12.5 grammes for the left, a ratio of 1.096 : 1. For the nine minutes after the spreading of the fingers of the right hand, the flow for this hand is 11.8 and for the left hand 10.4, a ratio of 1.134 : 1. The spreading of the fingers has therefore sensibly increased the quantity of heat given off. Nevertheless, even if this precaution is not adopted the error is not sufficiently great to seriously effect the accuracy of the result. This is of some consequence as there is nothing to trust to but the intelligence and zeal of the patient for the carrying out of the instruction to spread the fingers in the calorimeters.

The hands are kept in the bath for not less than ten minutes. Experiments specially directed to this point, of which the experiment summarized in Table I under M. C., 4 and 5 is an example, indicated that this length of time was sufficient for ordinary hands. The purpose of the pre-

liminary bath is to establish in the hand a steady distribution of temperature so that, when it is transferred to the calorimeter, the water in which is approximately at the same temperature as that of the bath, the changes of temperature which take place in the calorimeter owing to the presence of the hand shall be due wholly to the passage of blood through the hand and not in any sensible measure to the continued cooling of the tissues of the hand.

On the signal being given, the patient withdraws his hand from the bath. The wrists are rapidly dried. He seats himself quickly in the high chair and at once inserts his hand into the calorimeter, the hands being guided by the observer so as to obviate any risk of breaking the thermometers. Once the hands are inside the calorimeters the thermometers cannot be broken.

The blood flow in the fingers in proportion to their bulk seems to be more active than in the hand as a whole as is indicated in Experiment III on M. C., whose right hand was inserted into the calorimeter so far as to displace somewhat more than half the water displaced by the whole hand.

Experiment III.

Time.

11.37 a.m.	Right hand put in bath. Room temperature 22.2°.		
11.44	Temperature of bath is now 29.6°.		
11.47	Hand put in one calorimeter (R) (subject sitting) the other filled to give the rate of cooling. 30.50 c.c. water in each.		
	R.	L.	
11.46	29.47 (before hand put in)	29.59	
11.48	29.47		
11.49	29.50		
11.51	29.70		
11.52	29.77	29.55	
11.53	29.88		
11.54		29.53	
11.55	30.06		
11.56	30.12		
11.57	30.19		
11.58	30.26		
11.59	30.36 Hand taken out.		
12.01		29.45	Room 22.5°
12.06	30.285		
12.15	30.19		

Volume of hand in calorimeter 245c.c., pulse 100, rectal temperature 37.4°. From these data the flow calculated is 20.99 grammes of blood per 100c.c. hand substance per minute, which, as shown in Table I, is considerably greater than the average flow through the hand as a whole.

The exact time of immersion of the hands is noted, although this is not really indispensable, as the temperature observations can be started at any time, and the blood flow reckoned from any temperature observation. As a check on possible errors, I am in the habit of reading both calorimeter thermometers half a minute to a minute before the insertion of the hands into the calorimeters. The collars are adjusted and then the observer has nothing to do but stir the calorimeters and read the thermometers from time to time. I generally read them each minute, so as to be able to see whether the flow is varying, but for many purposes this is by no means necessary. Usually, unless the experimental conditions are purposely changed (see Paper II on vasomotor reflexes), the ascent of the thermometers

is quite uniform unless, indeed, as may happen with an unintelligent patient, the hand occasionally touches a thermometer bulb. All such accidental errors in the readings are eliminated over the whole period of observation by the very simple device of taking the final reading after withdrawal of the hand from the calorimeter. The exact moment of withdrawal being noted and the orifice of the calorimeter instantly closed with a felt disc, the final reading is made after thorough stirring for fifteen or twenty seconds.

To the heat gained by the calorimeter, calculated from the rise of temperature of the water, must of course be added the heat lost by the calorimeter during the period for which the blood flow is being reckoned. This can be determined once for all for a series of calorimeter and room temperatures. But there is invariably an interval after the removal of the hands, while the hand volume and other data are being obtained, during which the rate of cooling can be estimated in each experiment.

Water equivalent of the calorimeter. A further addition must be made for the water equivalent of the calorimeter and for the heat gained by the hand itself as the temperature of the calorimeter rises.

The water equivalent of a calorimeter of the construction used, *i.e.* a calorimeter protected from loss of heat by insulating material, cannot be exactly determined in the way in which that of a thin copper vessel not surrounded by insulating material but with its outer surface polished and enclosed in another vessel whose inner surface is also polished to reduce the loss of heat by radiation can be estimated, *viz.*, by adding to a known mass of water at given temperature already in the calorimeter a known mass of water at a different temperature and determining the temperature of the resulting mixture, allowing if necessary for the loss of heat by radiation during the short period required for uniformity of temperature to be attained. An approximate result, however, was obtained by the method of mixture and this was checked by calculating the water equivalent of the interior vessel from the weight of metal in it.

Experiment IV.

Weight of calorimeter with thermometer, lens, stirrer and felt disc for closing the aperture, 2,410 grammes.

Calorimeter plus water added at room temperature 4,690 grammes.

Weight of water added, 2,280 grammes.

Room temperature 19.0. Temperature of water in calorimeter after ten minutes, with vigorous stirring from time to time, 18.88.

Added water at 46.15. The water was taken from a large bath in an Erlenmeyer flask, filled and sunk in the bath and kept there for several minutes with ample stirring. Very quickly dried the outside of the flask and emptied it rapidly into the calorimeter, immediately closing the orifice again with the felt disc. Stirred well while observing the thermometer. Maximum temperature of the mixture reached 26.16.

Weight of calorimeter after addition of the warm water, 5,540 grammes.

Weight of warm water added, 850 grammes.

$\therefore 850 (46.15 - 26.16) = 2,280 (26.16 - 18.88) + x (26.16 - 18.88).$

From which X , the water equivalent of the calorimeter, = 54 grammes.

In this experiment the water added was purposely taken at a temperature higher than was advantageous so as to get a lower limit below which the water equivalent could not lie. Also

the lid and the lateral surface of the calorimeter immediately below it would scarcely, in the short time required for mixture, withdraw any appreciable amount of the heat, since they were not in direct contact with the water. Now the metal in these parts of the calorimeter makes up about one-fourth of the whole. We must therefore, increase the result by one-third, making 72 grammes. A calculation of the water equivalent from the weight of the inside vessel of the calorimeter and the specific heat of copper gave 74 grammes.

To obtain a round number and to allow something for the unavoidable loss of heat the water equivalent of the calorimeter has been taken as 80 in the calculations. This is almost exactly the result obtained in Experiment V where the temperatures were chosen so as almost to eliminate an exchange of heat between calorimeter and room.

Experiment V.

2.50 p.m.. Weight of water a little below room temperature added to the calorimeter, 2,595 grammes.

	Temperature of Calorimeter.	Room.
2.55 p.m..	19.39	20.4
3.00	19.40	20.3

3.03 Completed the rapid addition of 872 grammes water at 30.01 degrees. The water was taken from a large bath in an Erlenmeyer flask suspended for ten minutes in the bath by soft string around its neck and completely immersed. The flask was constantly moved about in the bath. The temperature was taken immediately before pouring the water into the calorimeter by immersing the bulb of the thermometer in the flask while it was still completely submerged.

	Temperature of Calorimeter.	Room.
3.04 p.m..	22.01	
3.05	22.00	
3.06	22.00	
3.10	21.99	20.25

From which $872 (30.01 - 22.01) = 2,605 (22.01 - 19.40) + x (22.01 - 19.40)$ i.e.,
 $6,976 = 6,799 + 2.61 x$ ∴ $x = 67.8$.

In this experiment the metal not in contact with the water would amount to about one-sixth of the whole, as there was more water in the calorimeter than in Experiment IV. We must therefore add $\frac{1}{6} \times 80$ i.e. 13.5 to the result. This gives 81 grammes as the water equivalent.

It must be pointed out that, although it was not thought right to neglect this quantity altogether, an error of 50 per cent. in the water equivalent would cause an error of less than $1\frac{1}{2}$ per cent. in the calculations.

Water equivalent of the hand (determination of specific heat of hand).
 Of greater consequence is the water equivalent of the hand itself. Not knowing the specific heat of the hand as a whole and being unable to calculate it from the specific heats given for the various tissues, I determined the specific heat of a perfectly fresh hand temporarily borrowed from the body of a man accidentally killed. The body was that of a man in the prime of life, well nourished though not fat. Height 170 cm.. Estimated weight 170 pounds. The chief injury was to the skull and there was extensive intra-cranial though no external hæmorrhage. The hand was of good size and had a good though not excessive amount of subcutaneous fat. A short "sleeve" of skin having been dissected down from about an inch above the wrist to the joint, the hand was disarticulated. The skin flap, which was retained to enable the hand to be neatly replaced on the body, was cleaned of most of the subcutaneous fat. The skin was then brought close across the articu-

lation and carefully stitched so as to make this end of the preparation, with the aid of a little melted paraffin, perfectly watertight. Two strands of thin copper wire were passed through the pulp of the middle finger and a short loop tied on them for supporting the hand in the bath and calorimeter.

Experiment VI.

Weight of hand, 520 grammes.

11.30 a.m.. Put into the calorimeter 3,015 c.c. water at about 20 degrees. Closed calorimeter with a felt disc, stirred well and let it stand. The temperature was chosen a little below that of the room, so that when the hand was afterwards put into the calorimeter the calorimeter temperature might be such that exchange of heat with the room could be neglected.

12.01 p.m.. Immersed the hand in a large bath holding 25 litres of water at about 35.5 degrees. Added and withdrew a little water two or three times during the period of immersion so as to keep the temperature about 35 degrees. The hand was suspended by the loop, which passed over a glass rod resting on the rim of the bath. A shorter glass rod, just fitting the orifice of the calorimeter, was laid in readiness under the felt disc. The bath was kept well stirred and the hand moved about. The room temperature was read on a thermometer suspended near the calorimeter.

Time.	Calorimeter.	Bath.	Room.
12.22 p.m..		—	22.0
12.23	20.22		
12.37	20.26		
12.38	20.26	34.96	
12.39		34.89	

* 12.39½. Put hand rapidly into calorimeter. The short glass rod was previously withdrawn from under the felt disc and used to support the hand in the bath for a minute or two, being held in the observer's hand. In transferring it to the calorimeter most of the water ran off. This was facilitated by holding the hand for an instant over the bath.

Time.	Calorimeter.	Room.	Time.	Calorimeter.	Room.	Time.	Calorimeter.	Room.
12.40½	20.80	—	12.52	21.46	—	1.05	21.62	—
12.42	20.99	—	12.53	21.49	—	1.07	21.62	—
12.43	21.08	21.6	12.54	21.50	—	1.08	21.63	—
12.44	21.15	—	12.55	21.51	21.8	1.09	21.65	—
12.45	21.22	—	12.57	21.53	—	1.10	21.65	21.7
12.46	21.27	21.8	12.58	21.55	—	1.11	21.66	—
12.47	21.30	—	12.59	21.56	21.85	1.12	21.66	21.8
12.48	21.34	—	1.00	21.58	—	1.13	21.67	—
12.49	21.38	—	1.02	21.60	21.9	1.15	21.68	—
12.50	21.41	21.9						

Weight of the hand after the measurements, 520 grammes. Therefore, it did not absorb any water during immersion. Volume of hand, 460 c.c. Specific Gravity of hand $520 = 1.13$.

$$\text{Calculation of specific heat, } 520 \times x \times 13.21 = 3,095 \times 1.42 \text{ or } 6897.2 \quad x = 4394.9$$

$$\therefore x = 0.6398, \text{ say } 0.64.$$

This is without taking account of the fact that the rise of temperature of the calorimeter was still proceeding slowly when the hand had to be replaced on the body. The maximum, as the curve plotted in Fig. 5 shows, would probably not be more than 0.04 or 0.05° above the temperature actually reached. Taking it as 0.05° we get 0.66 as the specific heat. A further small correction ought to be made for the relative anæmia of the dead hand as compared with the living hand, for the specific heat of blood is higher than the average specific heat of the hand. This correction might increase the specific heat to nearly 0.7. This round number has always been taken as the specific heat of the living hand in the calculations. Assuming that the specific gravity of the hand is 1.13 we must multiply the volume by 1.13 \times 0.7, i.e., 0.79 or, say, 0.8 to obtain the water equivalent of the hand in grammes.

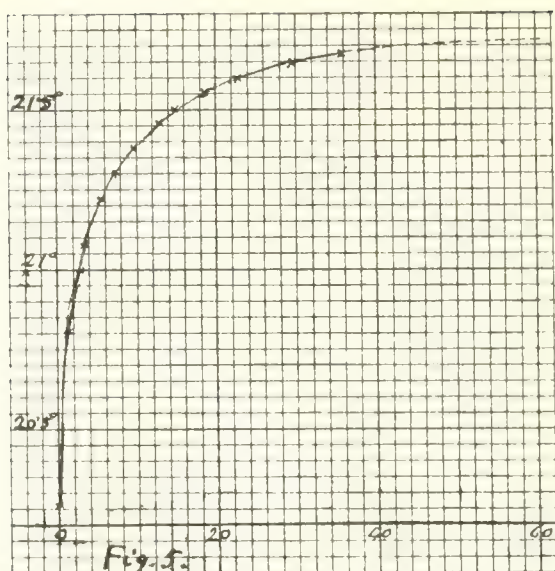


Fig. 5. Curve showing rising temperature of calorimeter in determination of specific heat of hand. Minutes plotted along horizontal, and degrees along vertical axis. Only the continuous part of the curve is plotted from actual readings as the hand had to be replaced on the body before the calorimeter temperature ceased to rise. The interrupted portion, however, as is obvious from the form of the curve, must approximately represent the further rise of temperature.

It has hitherto been tacitly assumed that all heat gained by the calorimeter comes from the blood flowing through the hand. This, of course, is not strictly correct for some heat is produced by the hand. It is not difficult to show, however, that in comparison with the heat lost by the blood this is negligible under ordinary conditions and within the limits of accuracy which it is expedient to aim at in such observations.

If we take the total heat production per hour of an average man on average diet during ordinary waking rest as 100,000 small calories (Atwater and Benedict) and the average weight of the hand as one one-hundred-and-fiftieth of the body weight (see Tables I and II), we get, on the assumption that the heat production of the resting hand is the average of that of the whole resting body, a production of 666 small calories per hour for the hand, or say, ten small calories per minute. The assumption that the heat production of the resting hand is equal to the average production of the resting body is certainly too liberal, since the proportion of relatively inactive tissue (bone, tendon, fascia and epidermis) is much greater and that of active tissue (muscle and glands) less than in the body as a whole. We shall hardly err on the side of under estimation if we take half this amount, say 5 small calories, as the heat production of the hand per minute. Now the average amount of heat lost by the hand per minute in an experiment with the initial temperature of the calorimeter of 30° varies from 100 small calories with a rather poor circulation to 200 with a fair circulation and to 400 with a good circulation. The error introduced by neglecting the heat production

of the hand would therefore with a medium circulation be no more than two and a half per cent. In hands with a feeble circulation it is probably but little greater since the poor peripheral circulation is itself unfavourable to a high rate of heat production.*

2. THE ESTIMATION OF T (THE TEMPERATURE OF THE ARTERIAL BLOOD COMING INTO THE HAND).

The average velocity of the arterial blood between the origin of the aorta and the crural artery in anesthetized dogs is usually less than 100 mm. per second as I have shown by an electrical method.⁹ Even if we assume that in a man sitting at rest the velocity is no greater than this, only five seconds would be consumed by the arterial blood in passing from the point where it leaves the shelter of the thorax to the wrist. The amount of cooling of the blood in a man sitting in a well warmed room with his arm covered by clothes might therefore *a priori* be assumed to be negligible for such observations as ours. But as we do not know the relation of the temperature of the blood in the left ventricle or aorta to that of any one of the cavities in which it is usual to measure the deep temperature, experiments were made to determine the actual temperature of the arterial blood at the wrist under the conditions of our blood flow observations. This was done in the following way:

In order to insure very slow cooling one of the calorimeters was packed in broken cork in a large can, the orifices in the lid being fitted temporarily with deeper rings to enable the extra layer of cork to cover the lid also. The room was purposely kept somewhat warmer than usual to reduce the loss of heat by the calorimeter. The calorimeter was filled in the ordinary way but with the water at a temperature a little above that of the interior of the body. The hand was immersed in the preparatory bath, as already described, and in due course transferred to the calorimeter. Readings of the temperature of the calorimeter were then taken regularly for a long time, with constant stirring, as the calorimeter slowly cooled. A similar series of readings was afterwards taken without the hand, the orifice of the calorimeter being closed with a felt disc. On correcting the first series of readings for the loss of heat from the calorimeter as determined by the second series, it could be seen of course that so long as the calorimeter temperature was above that of the arterial blood coming to the hand, the blood removed heat from the calorimeter since the venous blood left the hand at a higher temperature than the arterial blood had on entering it. Presently the point was reached at which the calorimeter ceased to either gain or lose heat. Leaving out of account the slight production of heat by the hand, it is clear that the calorimeter temperature, at which exchange of heat between hand and calorimeter ceases, must be the actual temperature of the blood in the arteries at the wrist. If no heat whatever were lost by the calorimeter (and no heat produced by the hand) the calorimeter would henceforth steadily maintain this

* In any case the local heat production tends to offset the under-estimation of the flow, as calculated from the formula, due to the fact that the venous blood does not quite acquire the temperature of the calorimeter.

temperature, so long as the temperature of the arterial blood itself did not alter. In the actual experiments, of course, the calorimeter still went on cooling below the temperature of the arterial blood although the fall of the calorimeter temperature was checked by loss of heat from blood to calorimeter as soon as the temperature of the calorimeter fell below that of the arterial blood, since now blood was entering the hand at a higher temperature than

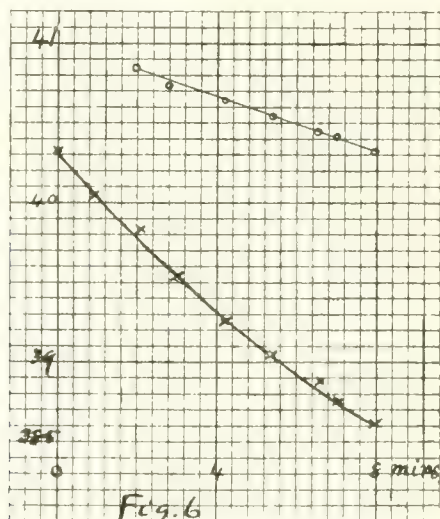


Fig. 6. Upper curve is the curve of cooling of the calorimeter when the hand is not in it, the lower curve the curve of cooling when the hand is in the calorimeter. Minutes laid off along horizontal and degrees along vertical axis (Experiment VII).

that of the venous blood issuing from it. These observations are illustrated by Experiments VII to X and by Fig. 6 to 11, which represent, plotted in various ways, the curves of cooling of the calorimeter when it contained and did not contain the hand.

In Experiment VII the initial temperature of the calorimeter was purposely made considerably higher than that of the arterial blood in order to demonstrate in a striking fashion the necessary loss of heat from calorimeter to blood when that condition was fulfilled. In this case the calorimeter was a much smaller one than that used in later experiments and was not arranged so as to cool particularly slowly. Fig. 6 shows graphically how much greater is the rate of cooling of the calorimeter when the hand is immersed in it (lower curve) than the rate when it does not contain the hand (upper curve). Even about 38.6° the lower curve is becoming less steep, although the experiment was not continued to the point corresponding to the temperature of the arterial blood, at which point the two curves would have become parallel. Although not specially suited for this purpose, the difference between the temperature of the calorimeter and that of the arterial blood not being sufficient for great accuracy, the experiment enables us to calculate

the blood flow through the hand at a temperature several degrees higher than the normal. It comes out, as could be predicted, much greater than the flow at temperatures below the normal, roughly speaking twice as great as the flow with the hand immersed in the water at 30°.

Experiment VII.

Left hand (S.) put into bath for five minutes and then into a calorimeter containing 1,200 c.c. of water. The initial temperature of the bath was 42.5 degrees and the temperature fell to 40.5° during the immersion of the hand. The calorimeter and another similar control calorimeter containing 1,550 c.c. of water were filled from the same bath. Two minutes after transference of the hand from the calorimeter, readings were begun. The subject was sitting.

Time.	Calorimeter containing hand.	Control Calorimeter.
2.00 p.m..	40.32	40.95*
2.00 $\frac{1}{2}$	40.04	40.90
2.02	39.84	40.85
2.03	39.54	40.75
2.04 $\frac{1}{2}$	39.24	40.65
2.05 $\frac{1}{2}$	39.09	40.55
2.06 $\frac{1}{2}$	38.89	40.45
2.07	38.76	40.40
2.08	38.64	40.30

Mouth temperature, 36.5°. Volume of hand in calorimeter, 350 c.c.. Taking the water equivalent of the hand and calorimeter as 300, and correcting for the loss of heat by the calorimeter, we get 725 small calories as the heat removed from the calorimeter by the blood passing through the hand in the last five minutes of the experiment. Taking the temperature of the arterial blood at the wrist as 36.5°, we get $750 \times 10 = 64.1$ grammes for the flow through the hand per minute,

$$5 \times 2.6 \quad 9$$

i.e., 18.3 grammes per 100 c.c. of hand per minute.†

In Table I. the results are summarized under S. 3.

In Experiment VIII, as shown in Fig. 7, the curve of cooling of the calorimeter when the hand is immersed in it (lower curve) becomes parallel to the curve of cooling without the hand (upper curve) at a calorimeter

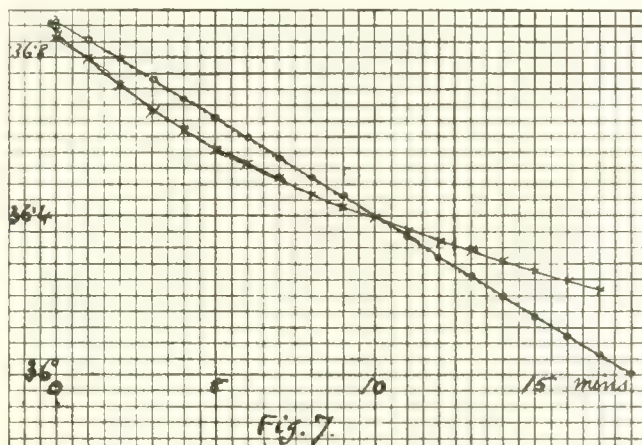


Fig. 7. Curves of cooling of calorimeter with and without hand (Experiment VIII). The latter curve is almost a straight line.

* The thermometer in this calorimeter was only sensitive to 0.05°.

† Since the difference between the average temperature of the calorimeter (39.09°) and the temperature of the arterial blood is only 2.6° the accuracy of this result is less than in any of the experiments solely directed to the determination of the blood flow.

temperature of 36.67° . At 36.63° it is still parallel, while at 36.57° it is already beginning to bend towards the upper curve. The temperature of the blood in the wrist arteries in this case may therefore be taken as 36.67° .

Experiment VIII.

2.19 p.m. Left hand (M. C.) put in bath at 38.3° .

2.23. Temperature of bath is now 38.0° . Room temperature 20.0° . 2,800 c.c. water in each calorimeter. (The calorimeters are not the same as were used in Experiment VII or Experiments IX and X).

2.24. Put left hand into calorimeter (subject sitting).

Time.	Calorimeter containing hand.	Control Calorimeter.	Time.	Calorimeter containing hand.	Control Calorimeter.
2.24	36.94 (just before hand put in)	37.00*	2.33	36.46	36.45
2.25	36.85	36.85	2.34	36.43	36.40
2.26	36.80	36.80	2.35	36.40	36.35
2.27	36.74	36.75	2.36	36.37	36.30
2.28	36.67	36.70	2.37	36.34	36.25
2.29	36.63	36.65	2.38	36.32	36.20
2.30	36.57	36.60	2.39	36.29	36.15
2.31	36.54	36.55	2.40	36.27	36.10
2.32	36.51	36.50	2.41	36.24	36.05
			2.42	36.22	36.00

In Experiment IX made with the doubly packed calorimeter, the two curves (Fig. 8) were about to become parallel at 36.70° , which was the

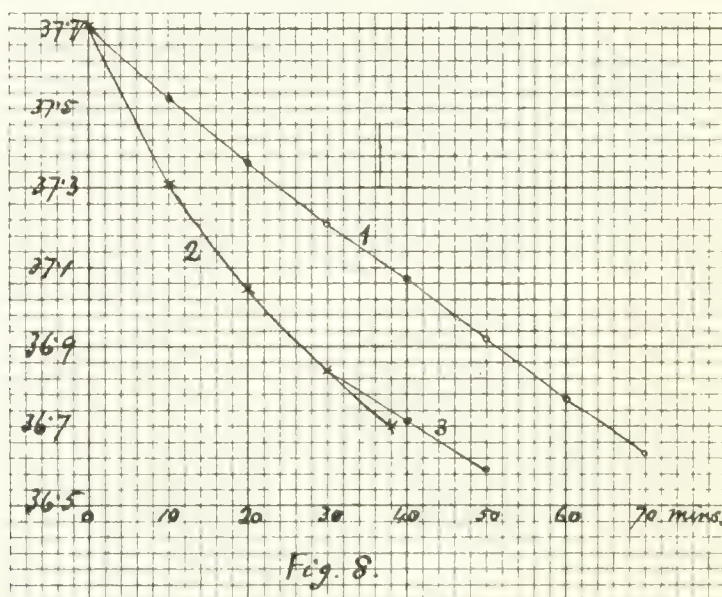


Fig. 8. Curves of cooling of calorimeter (doubly packed) with (2) and without (1) the hand (Experiment IX). 3 is the portion of 1 which corresponds to the point on 2 from which it starts.

* The thermometer in this calorimeter was sensitive only to 0.05° .

temperature of the calorimeter when the observations were stopped. At 36.84° there is still an angle formed between the curves, although it is much more acute than the angle formed at 37.70°. We can conclude that 36.70° cannot be far from the temperature of the arterial blood in this experiment.

Experiment IX.

Time.								
12.00 M.	Right hand (M.C.) put into bath at 39.0°. 3050 c.c. water put into calorimeter.							
12.10	Right hand put into doubly packed calorimeter (subject standing).							
	Calorimeter.	Room.	Time.	Calorimeter.	Room.	Time.	Calorimeter.	Room.
12.09	37.86		12.48	36.73	-	1.40	37.43	-
12.12	37.71	24.8	12.49	36.71	-	1.42	37.40	-
12.13	37.66	-	12.50	36.70	-	1.43	37.38	-
12.14	37.62	-	12.50½	Hand taken out.		1.44	37.37	24.9
12.15	37.57	-	12.54	36.60	24.9	1.45	37.36	-
12.16	37.52	-	12.57	36.56	-	1.46	37.33	-
12.17	37.48	24.9	1.00	36.51	-	1.48	37.30	-
12.18	37.45	-	1.02	36.48	-	1.49	37.28	-
12.19	37.40	-	1.03	36.45	-	1.50	37.27	-
12.20	37.37	-	1.05	36.43	24.9	1.52	37.25	-
12.21	37.33	-	1.06	36.41	-	1.53	37.23	-
12.22	37.31	-	1.07	36.38	-	1.54	37.21	-
12.23	37.28	-	1.08	36.38	-	1.55	37.19	-
12.24	37.26	24.9	1.09	36.36	-	1.56	37.18	25.0
12.26	37.20	-	1.10	36.36	-	1.58	37.15	-
12.27	37.17	-	1.12	36.32	-	2.00	37.13	-
12.28	37.14	-	1.13	36.29	-	2.03	37.09	25.1
12.29	37.12	-	1.16	Added 350 c.c. water at about 50°, to calorimeter and stirred up well.		2.05	37.06	-
12.30	37.10	-				2.07	37.02	24.8
12.31	37.08	-				2.09	36.99	-
12.33	37.02	-				2.11	36.97	-
12.34	37.00	-	1.20	37.78	25.0	2.13	36.93	25.0
12.35	36.98	-	1.21	37.78	-	2.15	36.91	-
12.36	36.96	-	1.22	37.76	-	2.17	36.87	-
12.37	36.94	24.9	1.24	37.71	-	2.19	36.85	24.9
12.38	36.92	-	1.26	37.68	-	2.21	36.82	-
12.39	36.90	-	1.27	37.67	24.95	2.23	36.79	24.6
12.40	36.88	-	1.29	37.63	-	2.25	36.76	-
12.41	36.86	-	1.30	37.61	-	2.27	36.73	24.9
12.42	36.84	-	1.31	37.59	-	2.29	36.71	-
12.44	36.81	-	1.33	37.56	-	2.30	36.69	-
12.45	36.79	-	1.35	37.51	-	3.20	36.09	25.1
12.46	36.77	-	1.37	37.48	-			
12.47	36.75	-	1.39	37.45	24.8			

The last observation was taken without stirring after 2.30, except for a minute or two immediately before reading the thermometer. In all the other observations the calorimeter was stirred practically continuously, as in the observations with the hand in the calorimeter.

At 1.07 p.m. temperature in mouth is 36.5°, in rectum 37.4°. Volume of hand inside the calorimeter 490 c.c. Pulse 100 (standing). The arm was bare up to the middle of the forearm while the hand was in the calorimeter.

The best experiment of the series is Experiment X, for here the observations were carried right through the "dead point" of the calorimeter temperature and continued for some time after it had been reached.

Experiment X.

Time.								
2.47 p.m.	Right hand of M. C. put into bath at 38.2°. 3,000 c.c. water put into (doubly packed) calorimeter.							
2.55	Temperature of bath is now 38.0.							
3.00	Right hand put into calorimeter (subject sitting).							
	Calorimeter.	Room.	Time.	Calorimeter.	Room.	Time.	Calorimeter.	Room.
2.59	37.59		3.39	36.66		4.31	36.96	
3.02	37.425		3.40	36.64		4.33	36.92	25.2
3.03	37.38	26.1	3.41	36.63	24.8	4.34	36.91	—
3.04	37.35	—	3.43	36.60	—	4.35	36.89	—
3.05	37.32	—	3.44	36.59	—	4.37	36.87	—
3.06	37.29	—	3.45	36.58	24.7	4.40	36.82	25.1
3.07	37.27	—	3.47	36.56	—	4.44	36.78	—
3.08	37.23	—	3.48	36.55	—	4.46	36.75	25.1
3.09	37.20	25.9	3.49	36.54	24.55	4.48	36.73	25.0
3.10	37.18	—	3.50	36.52	—	4.50	36.70	—
3.12	37.13	—	3.51	36.51	—	4.52	36.68	24.9
3.13	37.11	—	3.52	36.50	—	4.53	36.67	—
3.14	37.08	25.6	3.53	36.495	24.5	4.55	36.63	24.9
3.16	37.04	—	3.55	36.47	—	4.57	36.61	24.85
3.17	37.01	—	3.56	36.465	24.5	4.59	36.59	24.8
3.18	36.99	—	3.57	36.46	—	5.01	36.57	24.7
3.19	36.97	25.4	3.58	36.44	—	5.03	36.54	24.45
3.20	36.96	—	3.59	36.43	—	5.05	36.52	24.15
3.21	36.93	—	4.00	36.42	24.9	5.07	36.49	24.1
3.22	36.91	—	4.02	36.40	—	5.09	36.46	24.25
3.23	36.90	25.2	4.03	36.40	—	5.11	36.43	24.8
3.24	36.88	—	4.04	36.39	—	5.13	36.42	25.1
3.25	36.86	25.15	4.05	36.38	—	5.15	36.40	25.2
3.27	36.82	25.1	4.06	36.375	—	5.17	36.37	25.25
3.28	36.80	—	4.07	36.37	—	5.19	36.35	25.25
3.29	36.79	25.1	4.08	36.365	24.75	5.20	36.34	25.25
3.30	36.78	—	4.10	36.34	—			
3.31	36.77	—	Hand taken out of Calorimeter			Pulse, 96 (sitting).		
3.32	36.76	—	4.17 Added 350 c.c. water			Mouth temperature, 36.5°.		
3.33	36.73	24.9	(at 45°) to calorimeter.			Rectal temperature, 37.25°.		
3.35	36.70	—	Mixed well.			Axilla temperature, 36.35°.		
3.36	36.69	—	4.25	37.03	25.45	(All taken between 4.10 and		
3.37	36.68	24.7	4.27	36.995	—	4.20 p.m.).		
3.38	36.67	24.8	4.29	36.98	25.35	Volume of hand, 490 c.c..		

The results are graphically treated in Fig. 9 and 10. In Fig. 9 it is seen that at calorimeter temperature 36.90° the curve of cooling of the calorimeter with hand inserted is still descending somewhat more steeply than the curve of cooling of the calorimeter without the hand. Between 36.73° and 36.60° the two curves coincide, while below 36.60° the curve of cooling with the hand is less steep than that without the hand. The temperature of the arterial blood coming to the hand is therefore certainly neither higher than 36.73° nor lower than 36.60°.

In Fig. 10 the same thing is shown in a different way. Along the vertical axis are plotted the number of small calories per minute abstracted from (above the interrupted horizontal axis) or given off to (below the interrupted line) the calorimeter by the hand. Along the horizontal axis are plotted the temperatures of the calorimeter. Curve 2 is the curve of

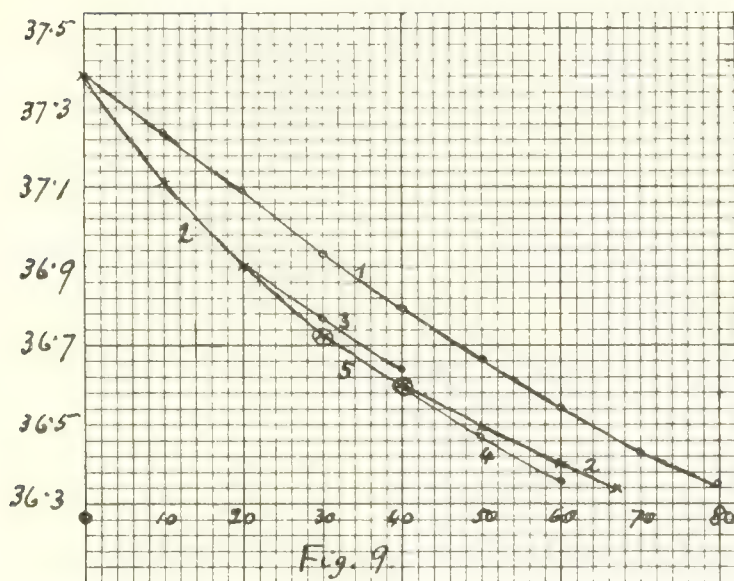


Fig. 9. Curves of cooling of calorimeter (doubly packed) with (2) and without (1) the hand (Experiment X). 3 is the portion of 1 which corresponds to the point on 2 from which it starts. The angle between 3 and 2 is much narrower than that between 1 and 2, showing that here the two curves are about to become parallel. For the stretch between the points indicated by the cross in the circle (5) they actually coincide, showing that the temperature of the arterial blood lies somewhere on this part of the curve. Below this the curve of cooling of the calorimeter without the hand (4) again forms an angle with 2 but on the opposite side of it from that formed by 3, showing that now the hand is heating the calorimeter. Minutes laid off along horizontal and degrees along vertical axis.

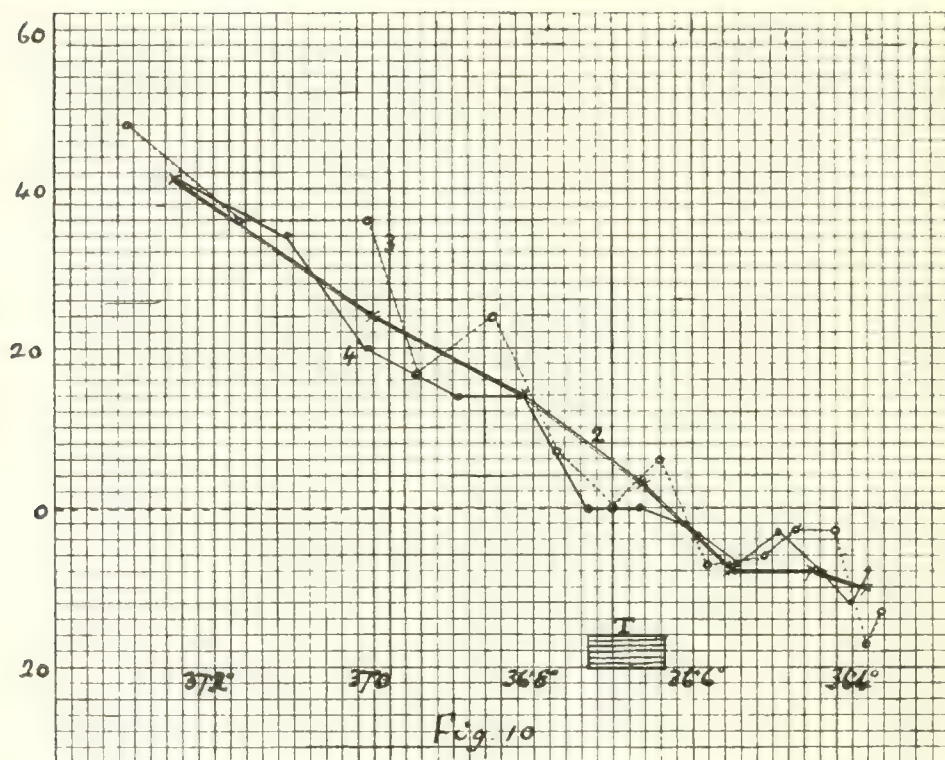


Fig. 10. The heat (in small calories) lost or gained by the hand in the calorimeter (in Experiment X) is plotted along the vertical axis and the calorimeter temperatures along the horizontal axis. Heat lost by the hand to the calorimeter is plotted below the interrupted zero line, heat lost by the calorimeter to the hand above the zero (0) line. The temperature corresponding to the point at which the curve crosses the zero line must represent the temperature of the arterial blood. For explanation of curves 2, 3 and 4, see text. *T* indicates the range of temperature within which the three curves cross the zero line.

heat exchange obtained by using the observations taken at each tenth minute. Curve 3 is a corresponding curve in which the observations taken at each fifth minute are used. Curve 4 is constructed in the same way as 2, but the ten-minute periods start with different minutes. In Fig. 11 the curve of heat exchange of Experiment IX (Curve 1) is shown over-

CURVE 1. (Exp. IX, Fig. 11.)

CURVE 2. (Exp. X, Fig. 10.)

Time.	Mean temperature of calorimeter.	Small calories gained from or lost to hand by calorimeter.		Time.	Mean temperature of calorimeter.	Small calories gained from or lost to hand by calorimeter.	
		In 10 min.	In one min.			In 10 min.	In one min.
12.12-12.15	37.64		- 127	3.03-3.13	37.25	- 408	- 41
12.15-12.20	37.47		- 77	3.13-3.23	37.00	- 238	- 24
12.20-12.25	37.30		- 41	3.23-3.33	36.81	- 136	- 14
12.25-12.30	37.165		- 39	3.33-3.43	36.66	- 34	- 3
12.30-12.35	37.04		- 34	3.43-3.53	36.55	- 85	- 8
12.35-12.40	36.93		- 18	3.53-4.03	36.45	- 85	- 8
12.40-12.45	36.835		- 12	4.00-4.10	36.38	- 102	- 10
12.45-12.50	36.745		- 12				

CURVE 3. (Exp. X, Fig. 10.)				CURVE 4. (Exp. X, Fig. 10.)			
3.03-3.08	37.305		18	3.03-3.13	37.245	108	41
3.08-3.13	37.17		36	3.08-3.18	37.11	340	34
3.13-3.18	37.05	- 36		3.13-3.23	37.005	204	20
3.18-3.23	36.945	- 17		3.18-3.28	36.895	136	14
3.23-3.28	36.85	24		3.23-3.33	36.815	136	14
3.28-3.33	36.77	7		3.28-3.38	36.735	0	0
3.33-3.38	36.70	0		3.33-3.43	36.665	0	0
3.38-3.43	36.64	6		3.38-3.48	36.61	- 17	- 2
3.43-3.48	36.58	- 7		3.43-3.53	36.55	- 68	- 7
3.48-3.53	36.51	- 6		3.48-3.58	36.495	34	3
3.53-3.58	36.47	- 3		3.53-4.03	36.445	- 85	- 8
3.58-4.03	36.42	- 3		3.58-4.08	36.40	- 119	- 12
4.03-4.08	36.38	- 17		4.00-4.10	36.38	85	8
4.05-4.10	36.36	- 13					

indicates loss of heat by calorimeter to hand; - indicates gain of heat by calorimeter from hand.

lapping Curve 2 of Fig. 10. No attempt has been made to draw smooth curves, but it is obvious that Curve 2 is much smoother than the other two, no doubt because the accidental variations in the minute readings are better eliminated. The irregularities in 3 and 4 are really insignificant but are greatly exaggerated in the figure, because at these temperatures the amount of heat actually exchanged is very small. Thus, when only 20 small calories per minute are being given off by the blood, heat exchange has practically ceased, yet the difference between 20 and, say, 16 is represented by two of the small squares. In Fig. 11 it is well brought out how nearly the curves become parallel to the horizontal axis as they approach the zero line, in contrast to the steep fall while the calorimeter temperature is still considerably above that of the arterial blood. The temperature corresponding to the point at which the curves cut the interrupted line of zero exchange is the temperature of the arterial blood. For Curve 2, it is 36.64°. Curve 3 (Fig. 9) first reaches

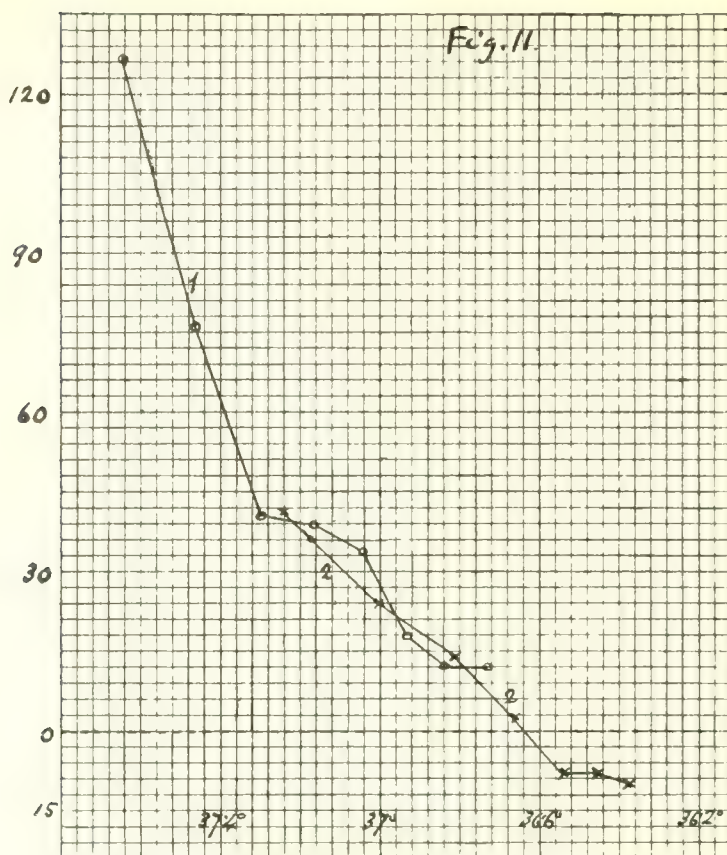


Fig. 11. Curve 2 of Fig. 10 is shown overlapping and continuing the curve (1) of heat exchange between hand and calorimeter in Experiment IX. Small calories along vertical and calorimeter temperatures along horizontal axis. The broken horizontal line is the line of no heat exchange.

the zero line at temperature 36.70° and Curve 4 at 36.73° . If we tabulate the arterial blood temperatures obtained on the same person (M. C.) at different dates the agreement becomes very striking.

November 12th, 1910	36.67	
January 4th, 1911	36.70	-
January 5th, 1911	36.73	-
	36.64	
	36.70	
	36.73	
	} average 36.70	
		36.60 + *

The average 36.70° is 0.55° below the rectal temperature on January 5th, and 0.7° below the rectal temperature on January 4th. It is 0.2° above the mouth temperatures on January 5th, and January 4th, and 0.35° above the axilla temperature on January 5th.

As it is, of course, out of the question to determine the temperature of the arterial blood by this method in each patient whose blood flow is being

*+ indicates that the number is below the true temperature, — that it is above it.

estimated, the question has to be settled how the internal temperature as clinically measured is to be corrected so as to give us the arterial temperature. The following rule has been adopted, which, if it seems a little arbitrary, can still introduce but a slight error. The main thing in any case is to have some fixed procedure, otherwise the results of different experiments would not be comparable. Where the rectal temperature and the mouth temperature can both be obtained and the mouth temperature is not more than 0.5° below the rectal, the mouth temperature is taken as that of the arterial blood at the wrist. Where the difference is greater than 0.5° , as is usual in M. C., the rectal temperature minus 0.5° is taken as the arterial blood temperature. Where only the mouth temperature can be got it is measured with as great care as possible, the thermometer being usually put back a second time, and then the mouth temperature is considered to be the arterial blood temperature. When the study of the blood flow in fever is taken up, the accuracy of this rule under abnormal temperature conditions must be checked by experimental determinations of the arterial blood temperature.

3. DETERMINATION OF T' (THE TEMPERATURE OF THE VENOUS BLOOD LEAVING THE HAND).

A consideration of the anatomical arrangement of the blood vessels of the hand indicates that when the part is immersed for a considerable time in water of given temperature, much the greater part of the venous blood must leave the hand at a temperature not very different from that of the bath. The hand (including the fingers) is a part whose surface is exceptionally great in proportion to its mass. It is also a member whose maximum thickness is small. The deeper tissues are much less vascular than the intermediate and the superficial structures. The hand indeed, consists of a bony scaffolding on which lies a thin layer of tissue containing nearly the whole blood supply of the part. Further, all the larger arteries and all the larger veins are very superficial. It was for these reasons that the hand was selected as the most favourable part in which to establish in the out-flowing venous blood a temperature which would be sensibly constant under the given conditions, and which could therefore be estimated without too great error. The foot, no doubt, comes next to the hand in this respect, particularly in children, and it is hoped later on to develop a calorimeter suitable for the foot.* In thicker parts, of course, if the average temperature of the issuing blood was known and could be made to remain sufficiently steady, or to vary in a calculable way throughout an experiment, the blood flow could equally well be calculated from the heat given off. It is, however, precisely this knowledge of the average temperature of the venous blood which is difficult to arrive at. In the case of the hand it was assumed that when the bath temperature and the period of immersion were properly chosen the error involved in taking the venous temperature as equal to that of the calorimeter could be neglected.

* With foot calorimeters constructed since this was written it has been found that the amount of heat given off per 100 c.c. of foot (in M.C.) is less than half the corresponding amount for the hand under the same conditions.

(1). Direct measurement of the temperature of the venous blood.

This assumption was shown to be permissible by directly measuring the temperature of blood obtained by puncture of a hand vein during immersion of the hand in a bath of known temperature. Suitable precautions were taken to avoid the loss of heat as far as possible and the actual loss was controlled by "dummy" experiments with water. The technique was as follows:

A small glass thimble with a capacity of 7 c.c. was surrounded by cork in a small beaker of capacity 50 c.c.. In the thimble a thin thermometer with a small bulb was supported through a bored cork. The beaker was slung in very thin wrapped wire, so that it could be at will let down into, or withdrawn from, a tall glass cylinder just wide enough to admit it freely. A large bath holding twenty-five litres was sterilized in a steam sterilizer. The glass cylinder and a large stirring spoon for the bath were also sterilized, and the bath was filled with sterile water at the required temperature. The cylinder, held in a clamp, was immersed deep in the bath and clean mercury poured into it so as to form a layer on the bottom of about 50 cm. in depth. The beaker, carrying the thimble and thermometer in position, was then lowered into the cylinder, where it rested on the top of the mercury. The mouth of the cylinder was closed with a plug of clean cotton. A sharp hypodermic needle of large bore was sterilized in oil in a test tube. The test tube containing a plug of cotton in the bottom, on which the point of the needle might rest, had been sterilized in the hot air oven before putting in the oil and needle. The needle passed through a small piece of cork which permitted the operator to handle it at a later stage without imparting heat to it from his fingers. During sterilization of the needle the test tube was heated on a sand bath. After sterilization most of the oil was poured out and the test tube closed with sterile cotton. It was then immersed in the bath by slipping over it two rubber bands previously introduced around the cylinder. These kept it fixed to the cylinder. The hand from which the blood was to be obtained was cleansed in the ordinary way and immersed in the bath. A thermometer was suspended in the bath and another near at hand in the air. As soon as the minimum period of immersion of the hand (usually ten minutes) had elapsed, the bath temperature, the air temperature and the temperature in the thimble were read. If the thimble temperature was not yet near that of the bath a further interval was allowed to elapse, the bath of course being frequently stirred. But since the thimble was usually put into the cylinder long before the immersion of the hand and watch was kept of the approximation of its temperature to that of the bath, the two were generally sufficiently near together, at the end of the normal period of immersion of the hand. The signal being then given, a folded towel was lightly twisted around the forearm so as to compress the veins, and then the operator, whose hands had been sterilized, rapidly withdrawing the needle from the test tube, punctured one of the veins on the back of the hand near the wrist, pushing the needle in toward the periphery. The tourniquet was instantly

withdrawn from the arm and blood collected in the thimble, which, enclosed in the small beaker, had been taken out of the cylinder at the moment of puncture. Usually the flow of blood was accelerated by pumping movements of the hand, as it was obvious that the only error which this could introduce would be to increase the observed excess of temperature of the venous blood over that of the bath as compared with the true excess during normal steady flow. If it turned out that even with the accelerated flow the excess was small, it would be certain that under normal conditions it must be still smaller and therefore negligible. Unless a flow of 4 or 5 c.c. of blood was obtained in forty or fifty seconds the experiment was not considered a good one. During the collection of the blood the thermometer, held by its supporting cork, was sloped within the orifice of the thimble, so that the blood first fell on the bulb as it dropped from the needle. The thimble, of course, remained always in its insulating covering in the beaker. The time from the beginning to the end of collection was noted. The moment enough blood had entered the thimble the thermometer was put in place, and the reading made with a lens. The thermometer was watched for some time longer and usually rose slightly (about 1-10 degree) for a few seconds after the cork was put in position. Having reached its maximum, it then sank very slowly owing to the good insulation of the cork. For the same reason the holding of the beaker in the hand could not sensibly heat the thimble, as was shown by a separate experiment.

To control the possible amount of heat lost by the blood in passing along the needle from the vein and dropping into the thimble, an experiment was always made with water after the collection of blood. In this all the temperature conditions were imitated as closely as possible and also the rate and time of out-flow. The bath itself was used as the source from which the water was drawn. This was accomplished by suspending in the bath the rubber bulb of a small enema syringe which, just before the collection of the water in the thimble, was filled and refilled from the bath, remaining all the time immersed in it. Connected with the bulb was a short rubber tube, which, in turn, was connected with the hypodermic needle. The thimble, in its beaker and fitted with its thermometer, was sunk in the glass cylinder just as in the actual experiment. When air temperature, thimble temperature and bath temperature corresponded as closely as was practicable to the temperature in the actual experiment, the beaker containing the thimble was taken out of the cylinder and an amount of water approximately equal to the amount of blood was made to fall by drops into the thimble at a rate as nearly as possible the same as that at which the blood had previously flowed. That is to say, the drops were slowed or accelerated from time to time so that the collection of the required quantity of water was completed in exactly the same time as that needed for the collection of the blood. The temperature of the water in the thimble was read and the difference between it and the bath temperature was taken as the measure of the unavoidable cooling during the collection of the blood. On adding this amount, which, of course,

was small when the experiment was carefully done, to the actually observed blood temperature, the true temperature of the venous blood as it flowed in the vein was supposed to be arrived at. Probably, however, the true correction ought to be somewhat smaller, since it was not practicable to collect the water without withdrawing a portion of the rubber tube, as well as the whole of the needle, from the bath, whereas in the collection of the blood there was nothing corresponding to the rubber tube to cool. A portion of the needle was imbedded in the skin, and a further portion lay in contact with the skin. Experiment XI is an example of one of these experiments. We had four which were considered successful, two of them carried out on the same individual at different times. A fifth experiment was only partially successful, the amount of blood obtained being too small (a little over 1 c.c.). Another experiment, the first one performed, was rejected because although the flow ultimately secured was sufficient, too long a time was occupied with the collection, owing to the withdrawal of the needle after the first puncture. In two experiments failure resulted because there was no flow of blood through the needle, probably owing to rapid clotting. This was before the sterilization of the needle in oil was resorted to. With our present experience it would probably be perfectly easy to secure an indefinitely large number of good observations, although cases might still be expected to be encountered, where, through faulty insertion of the needle, clotting, or the small size of the veins, the experiment would not succeed. But since the information sought had been obtained, there seemed no advantage in multiplying these experiments. The writer can vouch from personal experience that the little operation causes hardly any pain, and we have never seen the least harm result from it. A pad of sterile gauze secured by a bandage was worn over the puncture for twenty-four hours.

Experiment XI.

2.53 p.m.,	Right hand (of S.) put into bath.		
	BATH.	THIMBLE.	ROOM.
2.53	31.9	31.5	22.9
3.07	31.35	31.5	
3.13	31.35	31.45	

A little warm water was added to the bath at this point.

A vein on the back of the hand was now punctured but failed to yield any blood, perhaps because the needle had completely transixed the vein. Then another vein was punctured and a good flow obtained, the hand executing pumping movements. About 2 c.c. or 2.5 c.c. was allowed to escape before collection began. Then 4.5 c.c. was collected in 45 seconds, the greater part in the first 15 seconds and the rest more slowly in the remaining thirty seconds.

Temperature immediately after collection of the blood—

	BATH.	THIMBLE.	ROOM.
	31.3 falling	30.85 rising	24.2
	to 31.25	to 30.9	
3.21 p.m.,		30.9	—

Control experiments with water. First control experiment.

	BATH.	THIMBLE.	ROOM.
4.16 p.m.,	31.3	30.7	22.3
4.18	31.1	30.6	23.9

4.5 c.c. of water was now put into the thimble from the immersed rubber syringe, most of the water being allowed to flow into the thimble in fifteen seconds, the rest more slowly in the next thirty seconds. A good part of the rubber tube of the syringe projected above the water during the filling of the thimble. The reading of the thimble thermometer immediately after was 30.5°.

Second control experiment.

	BATH.	THIMBLE.	ROOM.
4.55 p.m.,	31.7	30.45	23.4

Now put 4.5 c.c. water into thimble from the immersed syringe, allowing the water to drop uniformly throughout 45 seconds. The temperature of the thimble is now 31.2°. Bath temperature immediately after is 31.6°. Room, 23.4°.

Third control experiment.

	BATH.	THIMBLE.	ROOM.
5.08 p.m.,	31.25	30.2	23.4
5.10	31.2	30.25	23.35

Now put 4.5 c.c. of water into thimble from the immersed syringe, allowing the greater part of it to flow in during the first fifteen seconds and the rest more slowly during the next thirty seconds, as in the blood experiment. The rubber tube of the syringe almost up to the needle was kept immersed during the filling of the thimble.

Temperature of thimble immediately after is 30.8° rising to 30.85°. 5.13½ p.m., Temperature of bath, 31.1°.

In the first control experiment the thimble temperature remains practically unchanged by the water from the syringe. The difference between the final thimble temperature and the bath temperature is therefore due to the cooling of the water on its way to the thimble. This difference, although the maximum for the three control experiments, is only 0.5°. If we add this to 30.9°, the final reading of the thimble thermometer in the blood experiment, we get 31.4° as the temperature of the blood in the vein, which is only 0.15° above the final reading of the bath.

It will be instructive to quote another experiment, made on a different person, in which although equality of temperature between thimble and bath was not waited for, a difference of 3 degrees still existing at the moment when the blood was obtained, practically the same result comes out when we allow in the calculation for the amount of the cooling of the blood by the thimble and thermometer.

Experiment XII.

Left hand of R. D. immersed for ten minutes in sterile bath. Temperature of bath 32.2°, of thimble 29.1°. Blood obtained from vein on back of hand. No tourniquet put on arm during insertion of needle. The flow was aided by contractions of the hand. In forty seconds 5 c.c. of blood was received into the thimble, the thermometer of which was then at once immersed in the blood. It read 31.3°, rising to 31.4° in sixty-three seconds from the time when the blood first began to fall on the bulb, i.e., about twenty-three seconds after the collection was ended. The hand was kept in the bath during the insertion of the needle and while the blood was being collected. Temperature of bath immediately after obtaining the blood, 32.2°. Room temperature, 22.2°.

*Control experiments with water.**First control experiment.*

BATH.	THIMBLE.	ROOM.
33.2	30.7	21.9

5 c.c. of water put into thimble from the immersed syringe in forty seconds. Maximum temperature of thimble now 32.2°

Second control experiment.

BATH.	THIMBLE.
32.3	29.2

5 c.c. water put into thimble, as in first experiment. Maximum reached by thimble, 30.9°. Bath just after filling thimble, 32.2°. Room, 22.5°.

In this experiment it is necessary to take account of the water equivalent of the thimble and thermometer since these are heated by the blood. The thimble weighed 3.3 grammes. The weight of the part of the thermometer stem immersed in the blood is 0.3 gramme. Total glass 3.6 grammes. Taking the specific heat of glass as 0.18, the water equivalent of the glass would be 0.64 gramme. The bulb of the thermometer displaced 0.25 c.c. of water and contained, say, 0.2 c.c. or 2.6 grammes of mercury. Taking the specific heat of mercury as 1.30 that of water, the mercury would have a water equivalent of 0.08 gramme. The total water equivalent of thimble and thermometer would thus be 0.72 gramme. But the upper third of the thimble, which was not in contact with the blood, would withdraw little heat from it, therefore 0.5 gramme would certainly be the maximum water equivalent, all the more as the glass even of the lower two thirds could not be uniformly heated throughout its thickness in the time of the temperature measurement. For simplicity let us take the water equivalent as 0.5. Assuming that the specific gravity of the blood is 1.060 and its specific heat 0.9, the cooling of 5 c.c. of blood by one degree would correspond to the withdrawal from it of 4.23 small calories. Thus we get

$$\frac{2.3 - 0.5}{4.23} = \text{or } 0.27, \text{ say, } 0.25$$

as the amount of cooling of the blood due to the heating of the thimble, etc., from 29.1° to 31.4°. The fall of the temperature due to the dropping through the air, etc., can be calculated from, say, the first control experiment. The temperature of the thimble was raised 1.5°, equivalent to the withdrawal of 0.5, 1.5, or 0.75 small calories, from the water, which would lower the temperature of 5 c.c. of water by 0.15°. But the temperature of the water was really lowered by one degree, therefore a fall of 0.85° must have been due to cooling before the water entered the thimble. No doubt, a portion of this was accounted for by cooling from the non-immersed parts of the syringe tube and connections not represented in the blood experiment. But to be sure that the correction is sufficiently liberal, let us take it at 0.8°. Then we get

$$31.4 \pm 0.25 \pm 0.8 = 32.45$$

as the temperature of the blood in the vein, an excess of 0.25° over the temperature of the bath.

It is clear that the greater the difference between the temperature of the bath and that of the arterial blood, the greater will be the permanent excess of the temperature of the venous blood over that of the bath. The experiments quoted show that for bath temperatures in the neighbourhood of 30° the error in taking the temperature of the venous blood as equal to that of the bath would not be more than $\frac{1}{3}$ or $\frac{1}{4}$ th of $T - T'$ (the difference between the temperatures of the arterial and venous blood in the formula for calculating the blood flow) or less than 4 per cent., which is negligible. As already pointed out, the approximation of venous temperature and bath temperature must be still closer when the blood flow is not abnormally accelerated by the movements of the hand (see also footnote p. 45.)

One experiment (Experiment XIII) was made on the leg of a dog. As was foreseen, the conditions were less favourable here than in the human hand for obtaining a close approximation of the temperature of the venous blood to that of the bath. Yet the experiment may be cited as probably giving a fair idea of the conditions which would be encountered in applying the method to the measurement of the blood flow in a large part of roughly cylindrical form like the human arm. It must be pointed out, however, that even here the result deduced on the assumption that the average temperature of the venous blood is the same as that of the bath would fix the *minimum* value below which the blood flow could not lie, a value for most purposes more important than a maximum value. When in the hand the

conditions, especially the temperature of the bath and calorimeter, are such that the average temperature of the venous blood, including the blood from the deep veins, must be appreciably higher than that of the bath, the blood flow calculated on the assumption that the two temperatures are the same is also necessarily less than the true flow. A correction could of course be applied, did we know the true temperature of the venous blood. For many purposes, however, and especially in comparative observations, the results are almost as useful when they give relative as when they give absolute values and, so far, the task has not been undertaken of attempting to fix the actual excess of temperature of the venous blood over that of the bath for a wide range of temperatures, or the difference between the temperature of the blood in the superficial veins and that coming from deeper parts. As already stated, the hand was chosen as the most favourable object because its shape, its dimensions and the situation of its blood vessels seemed almost *a priori* to eliminate the necessity of examining these questions for the purpose of the investigation. A comparison of the results obtained by the "stromuhr" on the limb of an animal with those yielded by the calorimetric method might enable the average temperature of the venous blood to be determined indirectly.

Experiment XIII.

A dog weighing 6.8 kilos was anesthetized with morphine and ether. It was a short haired animal, and the right leg was partially shaved below the middle of the thigh. A short glass cannula was inserted into the peripheral end of the *V. saphena magna* a little below its opening into the femoral vein. The right hind leg was immersed in a large bath at 22.2°. Room temperature, 22°. The beaker containing the thimble, as previously described, with the thermometer in place in the thimble, was immersed in the bath some time before, being pushed through a circular hole in a piece of wood floating in the bath and held in position in the hole by strips of sticking plaster. The temperature in the thimble having become nearly equal to that of the bath, some blood was collected from the vein. The temperature in the thimble rose to 25.4°, while that in the bath was 22.6°. As already explained, the lower the bath temperature the greater the excess of temperature of the venous blood must be for a given rate of flow.

(2) Further evidence showing that the temperature of the venous blood is near that of the bath is obtained when the blood flow in the hand of one and the same individual is measured with the bath at different temperatures, all, however, within that range which is subjectively indifferent to the hand, and so far as is known, incapable of causing reflex vaso-motor effects of any moment. When the other conditions are kept constant and only the bath temperature varies, it is found that the blood flow calculated on the assumption that the temperature of the venous blood is practically the same as that of the bath, comes out approximately the same for the different bath temperatures. This is seen particularly well when the two hands are immersed in water of different temperatures, of course within the range alluded to, and variations in the heart's action and changes in the general activity of the vaso-motor mechanism thus eliminated, as in Experiment XIV. It is, of course, mathematically possible that this result should follow if instead of the venous temperature being so near that of the bath in the different experiments that the difference is negligible, the excess of venous temperature over bath temperature is always the same fraction of the difference between the temperature of the arterial blood and that of the bath. If the fraction is made small enough, indeed, the two assumptions would yield the same result.

Experiment XIV.

TIME.				
12.13 p.m.	Put right hand of M. C. in bath at 29.0°, left hand in bath at 32.0°. Pulse (sitting) 88°. Mouth temperature, 36.63°. Rectal temperature, 37.0°.			
12.24	Hands put into calorimeters, right into R, left into L.			
	R	L	ROOM.	NOTES.
12.23	28.14	30.93		
12.26	28.37	31.02	20.5	Right hand feels distinctly colder than left.
12.27	28.49	31.11		
12.28	28.61	31.17	20.5	
12.29	28.70	31.24		
12.30	28.82	31.32		Right hand does not now feel so distinctly colder than left.
12.31	28.92	31.40		
12.32	29.02	31.43		
12.33	29.10	31.50	20.5	
12.34	29.24	31.57		
12.35	29.36	31.63		
12.36	29.48	31.70		Left hand still feels a little warmer than right when the fingers are moved, but not otherwise.
12.37	29.58	31.73	20.7	
12.38	29.67	31.82		
12.39	29.76	31.855		Hands taken out of calorimeters at 12.39.
12.39½	29.76	31.855		
12.47½	29.62	31.71	20.3	

From this experiment the following rates of flow can be calculated. For the right hand 13.66, for the left hand 13.48 grammes per 100 c.c. per minute (see Table I, M. C., 26) taking the temperature of the arterial blood as 36.5°.

The calorimeters were now emptied and an experiment (Experiment XV) performed on the same subject, but with both hands at approximately the same temperature as that of the left hand in the previous experiment.

Experiment XV.

Time.							
12.51½ p.m.	Put hands (M. C.) in bath at 32.1°.						
	R	L	ROOM.	TIME.	R	L	ROOM.
1.02	31.46	31.53		1.15	31.83	31.92	—
1.04	31.42	31.50		1.16	31.93	32.01	—
1.05½	31.39	31.49		1.17	31.98	32.04	20.9
1.07	31.37	31.46	—	1.18	32.04	32.10	—
1.08	Hands put in calorimeters.			1.19	32.10	32.15	—
1.10	31.48	31.56	20.9	1.20	32.17	32.23	20.8
1.11	31.57	31.67	—	Hands taken out of calorimeters.			
1.12	31.64	31.72	20.9	1.20½	32.17	32.23	—
1.13	31.71	31.80	—	1.25½	32.07	32.13	—
1.14	31.78	31.85	21.0	1.28½	32.02	32.09	—

From this experiment we get for the flow in the right hand 15.01 grammes and for the left hand 15.27 grammes per 100 c.c. per minute (see Table I,

M. C., 27). In both hands the flow is greater than in the previous experiment, but again it is practically equal in the two hands, the slight preponderance of the left being maintained.

In a third experiment (Experiment XVI), begun ten minutes later and with both hands at an initial temperature of a little below 29° in the calorimeters, and an average temperature of about 29.5° , a flow of 14.23 grammes per 100 c.c. per minute was obtained for the right hand, but only 10.85 grammes per 100 c.c. per minute for the left (for the first five minutes of the experiment) (Table I, M. C., 28). Here the discrepancy is unquestionably due to vaso-motor interference, which often shows itself after prolonged immersion, especially at the lower temperatures, by diminished blood flow and particularly by marked inequality of flow in the two hands. It was noticed by the subject during Experiment XVI that the left wrist felt colder than the right. In the light of experiments on the vaso-motor reflex effects to be cited later on, the result of the third experiment points to a moderate reflex vaso-constriction by the relatively cold water in the calorimeter, evoked especially from the left hand, perhaps by accidental wetting of the wrists and affecting the flow in both hands, although of course more markedly that in the left. For the next nine minutes of the experiment the flow comes out 11.84 grammes for the right, and 10.31 grammes per 100 c.c. per minute for the left, the increasing vaso-constriction beginning now distinctly to affect the right hand also. The next experiment (Experiment XVII), which was designed to test the effect of different bath and calorimeter temperatures on the flow, was vitiated for this purpose by reflex vaso-constrictor action, but may for this very reason be profitably quoted here, as it presents in an interesting way the marked influence of this factor and emphasizes the necessity of eliminating it as far as possible by properly choosing the conditions in comparative measurements of blood flow.

Experiment XVII.

3.23 p.m.. Hands (M. C.) put in bath at 30.2° . Mouth temperature, 36.5° . Rectal temperature, 37.1° . Pulse (sitting) 88.

TIME.	R	L	NOTES.
3.34	29.61	29.61	Room 21.1° .
3.35 $\frac{1}{2}$	-	-	Put hands in calorimeters. 3,015 c.c. water in each.
3.36	29.61	29.62	
3.37	29.70	29.69	
3.38	29.79	29.77	
3.39	29.89	29.86	
3.40	29.96	29.93	
3.41	30.03	30.01	
3.42	30.10	30.06	
3.43	30.18	30.14	
3.44	30.27	30.23	Now withdrew about 500 c.c. of water from L and replaced it by exactly the same amount of cold water, stirring well. The change was completed at 3.47 $\frac{1}{2}$ p.m..
3.48	30.43	27.56	
3.49	30.59	27.67	
3.50	30.66	27.80	
3.51	30.70	27.89	Room 21.5° .

Experiment XVII—continued.

TIME.	R	L	NOTES.
3.52	30.76	27.93	The right hand feels warm, the left cool.
3.53	30.80	28.01	
3.54	30.84	28.07	Now withdrew about 500 c.c. water from R and replaced it by exactly the same amount of cold water. Change complete at 3.56½ p.m.
3.57	28.03	28.37	Right hand now feels just a little cooler than left.
3.58	28.13	28.26	Room 21.5°.
3.59	28.21	28.31	Right wrist still feels colder than left, but fingers of both hands feel the same.
4.00	28.28	28.35	
4.01	28.33	28.39	
4.02	28.40	28.43	Right hand feels cooler than left.
4.03	28.45	28.46	
4.05	28.54	28.52	Now withdrew about 800 c.c. from each calorimeter and replaced it by exactly the same amount of warm water. Change complete at 4.10½ p.m.
4.11½	31.92	31.83	The hands feel warm and both the same.
4.12½	31.93	31.83	
4.14	31.94	31.82	
4.15	31.97	31.80	Room 20.2°.
4.16	31.98	31.80	
4.17	31.99	31.81	The hands feel comfortable but not very warm.
4.18	32.02	31.81	Left hand feels a little colder than right.
4.19	32.03	31.82	Room 21.0°.
4.20	32.06	31.83	
4.21	32.08	31.83	
4.22	32.10	31.84	
4.23	32.11	31.86	
4.24	32.13	31.87	
4.25	32.16	31.88	Hands taken out of calorimeters. Both collars slightly wet. Room 21.7°.
4.34	32.01	31.74	

Volume of right hand 470 c.c.. Volume of left, 460 c.c.. The marks were not quite symmetrically placed on the two hands, which accounts for the difference in their volume being smaller than usual. From the above data the blood flow comes out as follows:

Hand	Mean temperature of calorimeters.	H	T-T'	Q in grammes.	Number of minutes.	Blood flow per 100 c.c. of hand per minute
Right	29.94	2636	6.66	54.97	8	11.7
Left	29.93	2460	6.67	51.23	8	11.1
Right	30.64	1678	5.96	52.14	6	11.1
Left	27.82	2017	8.78	42.54	6	9.2
Right	28.29	2089	8.31	34.93	8	7.4
Left	28.36	1435	8.24	24.02	8	5.2
Right	32.07	1233	4.53	30.24	10	6.4
Left	31.84	854	4.76	19.93	10	4.3

It will be observed that there is a progressive decline in the blood flow, which is scarcely arrested, and in the case of the left hand is not arrested at all, even by a temperature of about 32°. There is little doubt that the reason of this is the vaso-constriction caused by the exposure of part of the previously immersed hand in the calorimeters while the water was being changed.

(3) *Relation between the skin temperature over a vein at the wrist and temperature of bath in which the hand is immersed.*—An interesting illustration of the manner in which the temperature of the venous blood follows that of the bath is afforded by measuring the skin temperature over one of the larger veins at the wrist by means of a thermometer whose bulb is covered with insulating material except where it touches the skin, while the hand is immersed in baths at various temperatures. Here the skin temperature is altered by conduction of heat through the structures between the thermometer and the lumen of the vein. The true temperature of the venous blood cannot of course be obtained in this way, since the surface temperature is affected also by conduction from the capillaries, arteries and the subjacent structures. Nor can the response to an alteration of the temperature in the bath be as prompt as the actual change of temperature in the blood of the superficial veins. Nevertheless, the fairly rapid and close correspondence between the temperature over the wrist vein and that of the bath makes it certain that the correspondence between the venous blood itself and the bath is still closer and more prompt. A protocol (of Experiment XVIII) will best illustrate the kind of data yielded by this method.

Experiment XVIII.

A small thermometer was attached by strips of sticking plaster on the left arm (of S.), with the bulb exactly over the beginning of the radial vein and the lower edge of the bulb just above the wrist point. Here the vein (of S.) which can be seen through the skin lies on bone and is not near any large artery. Hence the temperature of the skin over it is more likely to be easily affected by changes in the temperature of the blood in its lumen. The bulb was inserted into a small cork bored to fit it and then cut off flat at one side so as to expose this surface of the bulb, which was accurately in contact with the skin over the vein. Below, the hole in the cork was closed by cotton, cork and cotton being secured to the skin by sticking plaster. In other observations the hole was not bored right through the cork, and then the plug of cotton was not needed. By carefully applying the plaster it was not difficult to secure the thermometer so that it did not shift its position in the least during any ordinary manipulation of the arm and hand. Indeed, the observer could put on and off his laboratory coat, interrupt the experiment to attend to other duties, and return to it still wearing the thermometer quite undisturbed on the arm. This is mentioned to show that the changes of temperature indicated by the thermometer when the hand was put into the bath could not be due to the shifting of the bulb, but were certainly caused by changes in the temperature of the venous blood.

The small thermometer having become steady at 33.6° with the hand in the air, the hand was immersed in the large bath at 28.9° up to a level about two cm. below the bulb on the wrist. The temperature indicated by the small thermometer sank steadily to 29.6°, at which it remained constant. The hand was immersed for ten minutes, at the end of which time the bath temperature was still 28.9°. The hand was then taken out and the bath temperature made 25.7°. On immersion of the hand, the small thermometer became steady at 28.0°. With bath temperature 22.8°, the steady reading of the small thermometer was 25.4°. The bath temperature was now made 30.5°. At the moment of immersion of the hand the small thermometer read 25.4°, not having risen in the short interval since the last immersion (the baths were very rapidly prepared). In six minutes from the beginning of immersion of the hand the small thermometer rose to 30.5°. In three minutes more it read 31.0°.

Summary of experiment.

Bath.	Skin over wrist vein.	Difference.
28.9	29.6	0.7
25.7	28.0	2.3
22.8	25.4	2.6
30.5	31.0	+ 0.5

The change of temperature shown by the wrist thermometer is not in any important degree due to a reflex vaso-constriction in the wrist itself when the hand is immersed. For (a) a vaso-motor reflex induced in this way is a very rapid affair, as we shall see in the subsequent paper dealing with such changes in the blood flow of the hand. Now the adjustment of the wrist thermometer to the bath temperature is quite gradual. (b) A bath temperature of 29° or 30° , at which we find the steady reading of the wrist thermometer several degrees lower than the reading of the hand in air at ordinary room temperatures, does not cause any decided vaso-motor excitation. (c) A change in the rate of blood flow in the hand immersed in the bath can be shown to cause a small but definite change in the temperature over the wrist vein after it has been allowed to become steady. This is illustrated in Experiment XIX.

Experiment XIX.

The small thermometer was fastened as in the previous experiment, but on the right wrist of another subject (M. C.).

11.47 a.m. Hand put into bath at 31.2° . Room temperature, 22.9° .

Time.	Room.	Bath.	Skin over wrist vein.	
11.51			32.9	
12.06	21.7	30.9	32.5	
12.08			32.4	
12.09			32.55	After working hand for one minute.
12.11	21.3	30.8	32.25	
12.12			32.2	
12.13			32.1	After working hand $\frac{1}{2}$ minute.
12.14			32.2	After working hand $1\frac{1}{2}$ minutes.

Although the change is not great, the thermometer used enabled it to be detected with certainty. The first effect of causing the hand to execute pumping contractions is to reduce somewhat the temperature over the wrist vein. Then as the hand movements are continued the temperature rises again. The first effect is most easily explained as due to rapid passage along the radial vein of blood already contained in the hand veins and therefore at a lower temperature than the skin at the wrist. The second effect would be due to the increased circulation in the hand and therefore the increased inflow of relatively warm arterial blood, which has less time to cool in its passage through the hand than when the part is at rest. The first effect would not be seen in blood collected directly from a hand vein, as it is not due to actual lowering of the temperature of the blood passing through the vein but only to increase in the flow of relatively cool blood, which allows a greater amount of cooling of the skin of the wrist by conduction. This effect, accordingly, could not introduce any error in the experiments in which the temperature of the venous blood collected from the immersed hand during pumping contractions was directly measured. On the other hand, the second effect would tend to exaggerate the apparent excess of temperature

of the venous blood as compared with that of the bath. The experiment just quoted shows, then, that the observed excess of the venous blood directly collected is greater than the real excess although it does not enable us to say how much greater.

(4). *The slope of temperature in the hand with given bath temperatures and the time of immersion necessary for a steady state to be reached.*

Up to the present the question has not been discussed whether, granted that with a sufficient period of immersion in a bath the temperature of which is not too far from that of the arterial blood, the temperature of the blood in the superficial veins becomes practically the same as that of the bath, this can be assumed also without material error for the portion of the blood which issues by deeper veins. Connected with this question is the question of the slope of temperature from deeper to more superficial layers of the hand, once a steady state has been established with a bath of given temperature. It is, of course, perfectly clear that under two conditions the temperature can be made uniform throughout the hand and equal to that of the bath: (a) with circulation going on and bath temperature the same as that of the arterial blood; (b) with circulation stopped, the bath temperature being immaterial. The establishment of uniform temperature under the first condition has been already alluded to in connection with the determination of the actual temperature of the arterial blood. The rate at which uniform temperature is established under the second condition was studied on a hand obtained from the dissecting room, material not altogether suitable, but the best which could be got (Experiment XX).

Experiment XX.

A thin thermometer was pushed down from the wrist into the palm. After the experiment the position of the thermometer bulb was verified by cutting down on it. It lay between the flexor tendons of the index finger on the ulnar side and the muscles of the ball of the thumb on the radial side. The lower end of the bulb was at a level a little below the metacarpo-phalangeal joint of the thumb. The thickness of tissue over the bulb on the palmar aspect would vary from about 4 mm. to 8 mm..

2.06 p.m.. The thermometer in the hand, which had been lying near a window, was at 12.3°. The hand was now suspended by a fine copper wire in a large bath so that the level of the water was safely below the cut surface at the wrist. The initial temperature of the bath was 33.5°, with constant stirring, the following series of readings of the hand and bath thermometers was taken.

TIME.	HAND.	BATH.	TIME.	HAND.	BATH.
2.06	12.3	33.5	2.41	31.6	32.2
2.08	15.1		At 2.41 changed the water in the bath rapidly.		
2.09	16.5	33.4	One minute spent in changing it.		
2.11	19.0	33.4	2.49	31.3	24.1
2.13	21.2	33.3	2.51	29.9	24.1
2.15	23.1	33.2	2.53	28.8	24.1
2.17	24.9	33.2	2.55	27.9	24.0
2.19	26.2	33.1	2.57	27.2	24.0
2.21	27.3	33.0	2.59	26.5	24.0
2.23	28.2		3.01	25.9	23.9
2.27	30.1	32.7	3.03	25.6	23.9
2.30	30.9	32.6	3.06	25.1	23.9
2.33	31.2	32.4	3.10	24.6	23.8
2.37	31.45	32.3	3.13	24.3	23.8

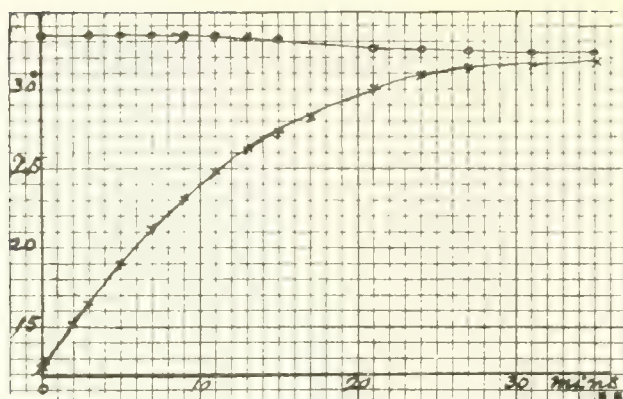


Fig. 12. Curve showing rate of conduction of heat through tissues of hand (Experiment XX). Degrees along vertical, minutes along horizontal axis. Upper curve, bath temperature; lower curve, temperature shown by thermometer inserted subcutaneously into a hand from the dissecting room immersed in the bath.

The results are graphically represented in Fig. 12. The upper curve gives the cooling of the bath and the lower the warming of the hand, which is at first rapid, then slower and slower as the bath temperature is approached. It will be seen that in 35 minutes a difference in temperature of 21.2° between hand and bath was reduced to 0.6° . A difference of 5.7° , which is probably quite as large a difference as normally exists between a layer of the living hand corresponding in depth to the position of the thermometer bulb and a bath at 30° , was reduced to 0.6° in 20 minutes, and in 12 minutes to 1.2° . The curve of heating of the calorimeter in Experiment VI on the specific heat of a fresh hand (Fig. 5) displays the same phenomenon, the flow of heat, as regards the hand, proceeding in the reverse direction.

To gain an idea of the length of time required for a steady distribution of temperature to be reached, with the circulation going on, Experiment XXI was made on the leg of a dog anesthetized by morphine and ether.

Experiment XXI

A thin thermometer was inserted through a slit in the skin of the right thigh, pushed well down in the subcutaneous tissue, and the skin then stitched with fine thread so as to fasten the thermometer in a pocket. The bulb was a little lower than the level of the knee. The hair of the animal was short and the right leg had been previously shaved below the middle of the thigh, so as to make the rate of cooling of the skin as nearly as possible the same as in the human hand.

At 4.05 p.m. the leg was immersed in a large bath at 22.3° , the bulb of the thermometer under the skin being well below the level of the water.

TIME.	THERMOMETER UNDER SKIN.	BATH.	DIFFERENCE.
4.06	26.4	22.3	4.1
4.08	26.5	22.4	4.1
4.09	26.4	22.4	4.0
4.10	25.6	22.4	3.2
4.11	25.4	-	3.0
4.12	25.3	22.4	2.9
4.12	25.1	22.5	2.6
4.14	24.8	22.5	2.3
4.15	24.5	22.6	1.9
4.17	24.3	22.7	1.6

Here in 12 minutes the excess of the subcutaneous temperature over the bath temperature was reduced to 1.6° . The rectal temperature at 4.20 p.m. was 34.6° . The animal had been anesthetized for more than an hour and used for a previous experiment. It was verified that no water had got into the pocket. The temperature between the toes of the right foot three minutes after removal from the bath was 22.5° .

Now inserted the thermometer bulb under the skin above the ankle joint of the left hind foot, the bulb being passed in through a slit well up on the leg and then pushed down. Closed the slit by stitches and bull dog clamps over the thermometer stem.

4.30 p.m., Immersed the left foot in bath.

TIME.	THERMOMETER UNDER SKIN.	BATH.	DIFFERENCE.
4.31	27.6	22.8	4.8
4.33	27.2	22.8	4.4
4.34	25.7	22.7	3.0
4.36	25.4		2.7
4.37	25.1	22.7	2.4
4.38	24.5	22.7	1.8
4.39	24.4		1.7
4.40	24.5	—	—

Here in nine minutes the excess of the subcutaneous temperature was reduced to 1.7° .

(5). *The length of time necessary for the living hand to assume a steady distribution of temperature.*

This can be estimated by using various periods of immersion for the hands of the same individual, all of the other conditions being as far as possible unchanged, and then determining the blood flow from the formula. Or, still better, the two hands can be immersed in the same bath for different lengths of time and the calculated blood flow compared. From observations of this kind it was concluded that ten minutes is, in general, a sufficient period of immersion in the preliminary bath. In addition, the readings for a little time after the insertion of the hands into the calorimeters are neglected while the "settling down" process, *i.e.*, the adjustment of the inevitable slight differences of temperature between hand and calorimeter is being completed. At least 12 minutes elapse from the beginning of immersion in the bath before calorimeter readings are taken which are used in the calculation, and often a longer interval. The main reason for not prolonging the preparatory bath is to save as much time as possible. For the same purpose the mouth temperature and, as a matter of routine, the pulse rate (in the neck) are generally taken while the hands are in the bath.

That an immersion period of ten minutes is sufficiently long was shown by immersing one hand in the bath and then, after an interval which varied in different experiments, immersing the other hand. The two hands were

then simultaneously inserted into the calorimeters. After the observations were completed, a new experiment was performed in which the hand subjected to the shorter period of immersion in the first experiment was now subjected to the longer, and *vice versa*. Experiment XXII, summarised in Table I under M. C., 4 and 5, is an example.

Experiment XXII.

First part of experiment.

2.04 p.m., Left hand put in bath at 23.7.
 2.09 Right hand put in bath at 23.7.
 2.11 Temperature of bath is 23.8.
 2.14 Hands put into calorimeters. Subject standing.

TIME.	CALORIMETER CONTAINING		TIME.	CALORIMETER CONTAINING	
	RIGHT HAND	LEFT HAND		RIGHT HAND	LEFT HAND
2.13	23.35	23.29	2.20	24.15	24.04
2.15	23.40	23.34	2.21	24.35	24.16
2.16	23.55	23.45	2.22	24.50	24.29
2.17	23.70	23.64	2.23	24.65	24.42
2.18	23.85	23.79	2.24	24.85	24.53
2.19	24.00	23.94	2.25	25.00	24.61

Rectal temperature 37.0. The quantity of water in each calorimeter was 2,800 c.c. Volume of right hand in calorimeter, 435 c.c. Volume of left hand, 420 c.c. The calorimeters were smaller than those subsequently used, and a smaller proportion of the hand could be inserted. Taking the water equivalent of hand and calorimeter as 400, and allowing 0.12° for the cooling of the calorimeters, as can be reckoned from a previous experiment, we get for the left hand $\frac{4448}{10 \times 12.5} \times \frac{10}{9} = 39.5$ grammes blood per minute or 9.4 grammes per 100 c.c. of hand per minute, and for the right hand $\frac{5504}{10 \times 12.3} \times \frac{10}{9} = 49.1$ grammes per minute, or 11.3 grammes per 100 c.c. per minute, taking 36.5° as the temperature of the arterial blood.

Second part of experiment

2.36 p.m., Room temperature, 20.5°. Pulse, 106.
 2.46 Right hand put in bath at 23.45°.
 2.51 Left hand put in bath at 23.45°.
 2.52 Temperature of bath is 23.65°.
 2.55 Temperature of bath, 23.78°.
 2.56 Hands put in calorimeters. 2,800 c.c. in each.

TIME.	CALORIMETER CONTAINING		TIME.	CALORIMETER CONTAINING	
	RIGHT HAND	LEFT HAND		RIGHT HAND	LEFT HAND
2.56	23.40*	23.44*	3.02	24.15	24.23
2.57	23.45	23.52	3.03	24.30	24.33
2.58	23.55	23.64	3.04	24.45	24.44
2.59	23.70	23.79	3.05	24.60	24.59
3.00	23.85	23.85	3.06	24.70	24.69
3.01	24.00	24.05	3.07	24.75	24.76

* Just before the hands were inserted.

From which we get for the left hand $\frac{4352}{10 \times 12.4} \times \frac{10}{9} = 39.0$ grammes blood per minute = 9.3 grammes per 100 c.c. per minute; and for the right hand $\frac{4544}{10 \times 12.4} \times \frac{10}{9} = 40.7$ grammes per minute = 9.4 grammes per 100 c.c. per minute.

In the first part of the experiment, where one hand was immersed in the preliminary bath for only five minutes and the other for ten minutes, there is a greater difference between the flow in the two hands in this individual than is normally the case when both hands are immersed for ten minutes. Considerable weight can be placed upon a difference of this amount because the person examined has been used very frequently in the investigation, and with very constant results. In the second part of the experiment the agreement between the hands is much closer, probably because in the short interval between the experiments the effects of the previous immersion had not entirely worn off. A five minutes immersion in the preparatory bath was therefore sufficient to produce the steady condition and to give practically the same flow in the left hand as the ten minutes immersion in the first.

The great importance of having the temperature conditions the same in observations which are to be compared with each other is well illustrated by Experiments XXIII and XXIV.

Experiment XXIII.

H. O. F. Age 34. Height 5 ft. 5 in.. Weight 124 lbs.. Healthy male. Pulse 66 (sitting). Rectal temperature 37.1°. Hands cold after a four mile drive in an automobile on a cold morning, and had not warmed up appreciably during the fifteen or twenty minutes he had been in the laboratory before the observations were begun. He stated that his hands were somewhat susceptible to cold. The veins were seen to be small both before immersion in the bath and after removal from the calorimeter. He still felt his hands cold at the end of the experiment.

9.50 a.m.. Hands put in bath at 30.0°. 3,050 c.c. water put in each calorimeter
10.04 Put hands in calorimeters, as usual right in R, left in L. (Subject sitting).

TIME.	R	L	TIME.	R	L
10.03	29.34	29.51	10.27	29.40	29.38
10.05	29.28	29.43	10.30	29.42	29.38
10.07	29.26	29.40	10.33	29.46	29.39
10.09	29.24	29.37	10.35	29.48	29.39
10.11	29.23	29.36	10.37	29.50	29.39
10.14	29.27	29.33	10.38	29.50	29.39
10.16	29.28	29.36	Hands removed from calorim.		
10.19	29.31	29.36	10.44	29.44	29.30
10.21	29.33	29.32	10.50	29.36	29.22
10.23	29.36	29.34	10.58	29.24	29.10
10.25	29.38	29.37	11.08	29.11	28.98

Right hand cooler, a little cooler than left.

Room 19.4. Volume of left hand in calorimeter, 340 c.c. Volume of right hand, 360 c.c.

For the last 27 minutes of the experiment the flow for the right hand is 12.06 grammes per minute, *i.e.*, 3.35 grammes per 100 c.c. of hand per minute; and for the left hand for the last 17 minutes 9.13 grammes per minute or 2.69 grammes per 100 c.c. of hand per minute, taking the arterial temperature as 36.6°.

Experiment XXIV.

The subject having now warmed up, at

12.42 p.m. the hands were again immersed in the bath at 30.2°. His hands are now normally warm, he says. On putting them into the bath he feels it cool, whereas in the morning he felt it warm. 3,050 c.c. put in each calorimeter. Room 24.0.

12.56 p.m.. Hands put into calorimeters.* (Subject sitting).

TIME.	R	L	TIME.	R	L	
12.53!	29.60	29.60	1.13	30.22	30.20	
12.58	29.60	29.70	1.14	30.26	30.21	
1.00	29.70	29.78	Hands removed from cal.			
1.03	29.83	29.88	1.20	30.22	30.14	Room 22.7
1.05	29.93	29.96	1.25	30.14	30.09	
1.07	30.04	30.04	1.28	30.11	30.05	
1.09	30.13	30.10	1.34	30.05	30.00	
1.11	30.18	30.16				

Rectal temperature, 37.3°. Pulse (sitting) 76.

From these data the flow per minute for sixteen minutes comes out 28.68 grammes per minute, or 7.97 grammes per 100 c.c. per minute for the right hand: and 23.49 grammes per minute, or 6.91 grammes per 100 c.c. per minute for the left hand, taking the arterial temperature as 36.8°.

4. SPECIFIC HEAT OF THE BLOOD.

For the specific heat of the blood the value 0.9 was used in all the calculations. H. Bordier,¹ gives as the results of a large number of observations the following values: arterial blood 0.901; defibrinated blood 0.920; serum 0.932. Comparative experiments on arterial and venous blood gave for arterial blood 0.906, and for venous blood 0.893. The larger the proportion of erythrocytes and the smaller the proportion of plasma, the smaller is the specific heat. In cases where the blood varies extremely from the normal in this respect, as in severe anemia or marked polycythemia, it might be worth while to make a correction in accordance with the blood count.

5. MEASUREMENT OF THE VOLUME OF THE HAND.

This was done by displacement, and with apparatus of the simplest kind and such as is easily procurable in clinical work. The hand was immersed to exactly the lower mark in a glass douche-can connected by a short rubber tube with a burette furnished with a side tube at its lower end. The hand was held hanging vertically down as in the calorimeter. Before immersion of the hand the douche-can was filled with water to a mark so that the initial level was the same in different experiments. This is advisable as the can may not be of quite uniform cross section. The lowest

* In all experiments, unless otherwise mentioned, the right hand was in calorimeter R and the left in calorimeter L.

graduation of the burette was also brought level with the water before the hand was immersed. On immersion the level of the water in the burette was read off. All that was necessary to get the volume of the hand was to pour water into the can from a graduated measure after withdrawal of the hand, until the same level was reached. The amount poured in obviously gives the volume of the hand. A few measurements of this kind, made once for all, permit the burette readings to be directly translated into hand volumes without repeating the measurements each time. The burette is simply used as a good scale, easily procurable. Adjustment of the burette can be quite exactly made by running a little water out of it or adding a little to the can while the scale is read by a lens. When the two hands are successively measured, the small amount of water withdrawn by the first is automatically restored by the second since it is put in wet.

RESULTS.

So far about thirty experiments have been made on six normal persons and about 45 experiments on 38 clinical cases. The latter included Raynaud's disease (two cases), birth palsy (one case), infantile paralysis (one case), hemiplegia (one case), Graves' disease (one case), progressive muscular atrophy (one case), unilateral peripheral neuritis (five cases), emphysema associated with cyanosis (one case six times examined), gastric dilatation with anæmia (one case), pleurisy with effusion (tubercular) (one case), nervous dyspepsia (one case), aortic incompetence and stenosis (one case), mitral insufficiency (two cases), thoracic aneurism (three cases), senile heart with arrhythmia and arterio-sclerosis (one case), tabes (one case), myocarditis (two cases), pulmonary tuberculosis (two cases), goitre with palpitation (not Graves' disease) (one case), oedema of hand (following division of radial nerve?) (one case), inflammation of hand due to infected finger (one case).

In many of these cases and in some of the normal subjects, in addition to simple measurements of the blood flow the changes produced in it by vaso-motor reactions, especially those elicited in one hand by changes of temperature in the other, were studied. The method seems to lend itself particularly well to a quantitative study of such vaso-motor reflexes in man. A much larger mass of material is being collected and will be dealt with in detail in a future paper or papers. In the meantime a summary of the results is presented in Tables I and II.

The changes in the blood flow in the hand produced through vaso-motor reflexes will be dealt with in somewhat greater detail than the others, in the short paper immediately following this. In addition, the influence on the flow of forced breathing, which diminishes it, and of the inhalation of oxygen, which in a case of emphysema with cyanosis was found to increase it, although it had no effect on a normal person, and of contraction of the hand muscles, which markedly increases it, has been to some extent investigated.

In the normal cases when measured under the standard conditions, viz., bath and calorimeter temperatures not far removed from 30°, ordinary room temperature, no unusual exposure to cold before the experiment, and a

moderate period of immersion in the calorimeter (10 to 15 minutes), did not exceed 14 grammes per 100 c.c. of hand per minute, nor fall below 3.5 grammes. For the whole posterior extremity, in dogs, Landergren and Tigerstedt⁵ and Tschuewsky¹⁰ give 5 c.c. per 100 grammes of tissue per minute for the flow as measured by the "Stromuhr."

The higher the room temperature the greater in general is the flow. When this factor is taken into account the results in one and the same individual on different days with similar calorimeter temperatures do not differ greatly, although different individuals when tested under apparently similar conditions show a much greater range in the blood flow. Some normal persons know and say that their hands are habitually cool or cold, others that their hands are habitually warm. The former will show a relatively small, and the latter a relatively large flow. Thus M. C. and C. B. work as laboratory assistants in the same laboratory, and E. W. as laboratory assistant in an adjoining laboratory. They are all, so far as is known, in good health, all young men and doing not very dissimilar work. Yet in winter at least M. C. habitually has a flow two to three times as great as was observed in the other two. It is true that only on one day were observations made on C. B. and E. W.. But among the numerous measurements on M. C. under normal conditions none falls anything like so low as those of the other two.

In the pathological group the extremely small flows in Mrs. A. (averaging the two hands, a little over 0.6 gramme per 100 c.c. per minute) and S. F. (only 0.2 gramme per 100 c.c. per minute) accord well with the actual conditions. Mrs. A., aged 72, showed the typical skinny hand of old age, with feeble pulse, marked cardiac arrhythmia and arterio-sclerosis. Obviously the hands were receiving but little blood. It must be noted also that the proportion of inactive and therefore comparatively bloodless tissue (bone, etc.) in a hand of this sort would doubtless be greater than in the hand of a young person. S. F. was suffering from myocarditis, with very pronounced cardiac arrhythmia.* He said his hands and feet were always cold. His pulse was feeble, and the rate had to be counted with the stethoscope on account of the arrhythmia. It was only 60. A large or even a normal flow could not exist under these circumstances.

The influence of the inhalation of oxygen on the flow was investigated in the case of S. G., since the mechanism of the recurring cyanosis in this patient, unaccompanied by dyspnoea, was in doubt. The opportunity was afforded during some experiments of my colleagues Drs. Hoover and Macleod on the partial pressure of carbon dioxide and oxygen in the alveolar air of this patient. A distinct increase in the flow was produced by oxygen, and this was accompanied by an increase in the amplitude and a diminution in the tension of the radial pulse, appreciable by the finger. A change was also observed in the sphygmogram, the amplitude of which was increased. (S. G.,

*He was admitted to the hospital on the day of the observations and died there a few days.

Experiments 4, 5, 6, Table II). The effect could not be due to any change in mechanics of the respiration produced by the mask employed. For (a) the total ventilation remained unchanged; (b) a moderate degree of forced respiration *diminished* the flow in two normal persons (M. C., 15, and C. B., 2, Table I). Oxygen produced no effect in two normal persons (M. C., 20, and E. W., 3, Table I). It is perhaps worth considering whether in other cyanotic conditions, as when administered in pneumonia for example, the action of oxygen is not in part an action on the vaso-motor mechanism which diminishes the resistance in the small vessels and so aids the blood flow.

That an increase in the flow is caused by muscular contractions of the hand is, of course, known. Yet it is interesting to have a quantitative expression of this increase. The experiment cited in Table I as M. C. 3, gave 15.4 grammes as the flow in the contracting hand per 100 c.c. per minute and only 4.9 grammes in the resting hand. A comparison of this with the other experiments on the same person shows that 4.9 grammes is much smaller than any flow recorded with the two hands under similar conditions. The increase in flow in the contracting hand is therefore accompanied by a reciprocal diminution in the flow in the resting hand.

The diminution in the flow caused by a moderate degree of pressure applied to the wrist by a rubber band was measured in the experiment referred to in Table I as S. 8. The flow which had been 13.2 grammes and 13.1 grammes respectively in two experiments immediately preceding the constriction (the numbers are high partly because this individual has a habitually good flow in the hands partly because of the high room temperature) was diminished to 4.2 grammes per 100 c.c. per minute for the first four minutes after constriction. For the next six minutes the flow rose to 11.3 grammes per 100 c.c. per minute, owing of course to the gradual rise of the venous pressure distal to the band, which enabled the obstruction to be more and more successfully overcome.

The influence of direct heating of the hand whose flow is being measured (*i.e.*, of a high bath and calorimeter temperature) is shown in the experiments cited in Table I as S. 1, 2 and 3. These give without exception the greatest blood flows observed, a fact easily explained by the marked vaso-dilator action of the high temperature.

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STUDIES ON THE CIRCULATION IN MAN.

II. THE EFFECT OF REFLEX VASO-MOTOR EXCITATION ON THE BLOOD FLOW IN THE HAND.

BY G. N. STEWART.

(From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, Cleveland).

THE changes produced in the circulation of one hand by eliciting vaso-motor reflexes from the other or from other parts of the body can be quantitatively studied with great ease by the calorimetric method. The following experiment (XXV) on a normal person illustrates the magnitude of the change which occurs in the blood flow in one hand when the other is exposed to cold or heat.

Experiment XXV.

2.46 p.m., Right hand (of M. C.) put into bath at 29.7°. 3,000 c.c. of water in calorimeter R.
2.57½ Right hand put into calorimeter. Room 18.8°.

TIME.	R	NOTES.	TIME.	R	NOTES.
2.57	28.84		3.29	30.70	
2.59	28.89		3.30	30.77	
3.00	28.98		3.31	30.82	
3.01	29.07		3.32	30.88	
3.02	29.18		3.33	30.94	At 3.33 left hand re-
3.03	29.29	Room 19.1			moved from the warm
3.04	29.39				water and dried.
3.05	29.49	At 3.05 immersed left	3.34	31.01	Room 20.15°.
3.06	29.54	hand in water at 7.4°.	3.35	31.08	
3.07	29.58	Room 19.1.	3.36	31.15	
3.08	29.62		3.37	31.19	At 3.37 left hand put in
3.09	29.66		3.38	31.22	water at 10°.
3.10	29.70		3.39	31.25	
3.11	29.74	At 3.11 took left hand	3.40	31.27	
		out of cold water,	3.41	31.29	
		dried and warmed it.	3.43	31.32	At 3.43 left hand trans-
		The subject was directed to put it in his	3.44	31.33	ferred to water at 42.5°
3.12½	29.80	pocket. Temperature	3.45	31.37	
3.13½	29.89	of cold water is now	3.46	31.39	
3.14½	29.95	9.7°.	3.47	31.42	
3.16	30.06		3.48	31.46	Room 20.6°.
3.17	30.13	He says left hand now	3.49	31.49	
		feels as warm as before	3.50	31.53	
		immersion in cold water	3.51	31.58	
3.19	30.27	Fingers of left hand, now	3.52	31.60	At 3.52 removed left
		through inadvertence,	3.53	31.62	hand from the warm
3.21	30.33	dipped into warm water	3.54	31.67	water and dried it.
3.22	30.38	and then with	3.55	31.70	
3.23	30.41	drawn.	3.56	31.72	
3.25	30.50	At 3.25 immersed left	3.57	31.73	Room 20.5°. At 3.57
3.26	30.53	hand in water at 43.0°			removed hand from
3.27	30.57				calorimeter.
3.28	30.63	Room 19.5°.	4.11	31.51	Room 19.7°.

Volume of right hand, 485 c.c.,
Mouth temperature, 36.55°.

Rectal temperature, 36.9°.
Pulse (sitting) 80.

From these data the calculated blood flow in the right hand (for the first six minutes of the experiment) is 12.67 grammes per 100 c.c. of hand per minute. This is at once reduced to 6.64 grammes per 100 c.c. of hand per minute (for the next six minutes) during the immersion of the other hand in cold water. Inspection of the minute readings shows that the change in the flow follows at once on exposure of the opposite hand to the cold water and is permanent for the duration of the observation (six minutes). It is of interest to note this behaviour of this contralateral vaso-motor reflex because in some pathological cases studied the reflex though prompt in onset was much more transient; in others it was slow in appearing; and in others still it could be only feebly elicited, or not at all.

After removal of the left hand from the cold water the flow in the right hand increases to 10.2 grammes per 100 c.c. per minute (for the first eight minutes). The minute readings of the protocol show that the increase is not apparent for the first one and a half minutes but is evident in two and a half minutes. The left hand was dried with a cloth to prevent continued cooling by evaporation, and thus to check, as far as possible, the reflex excitation. It is obvious that this could not be done at once, and it was six minutes before the hand felt to the subject himself as warm as before. The readings between 3.19 p.m. and 3.25 p.m. show an abrupt slackening in the rate of increase of the calorimeter temperature. For the six minute period the flow comes out at only 7.05 grammes per 100 c.c. per minute. The reason is instructive. A vessel of warm water, for use in the next part of the experiment, had been prepared and, being within reach of the subject, he carelessly dipped the fingers of the left hand into it once or twice and then withdrew them, holding them still wet in the air. There can hardly be any question that the sudden diminution in the flow in the right hand was caused by reflex vaso-constriction elicited from the wet and therefore cooling left hand. Had this circumstance not been observed, the sudden change in the rate of flow would have been puzzling. Immersion of the left hand in the warm water (at 43°) causes an increase in the flow in the right which is not obvious in the thermometric readings till two minutes have elapsed. It must be remembered, of course, that any change in the temperature sufficient to be read must lag somewhat behind the corresponding change in the blood flow. The amount of lag under the conditions of these experiments has not yet been determined, although this could easily be done by altering the flow suddenly by mechanical means, but it cannot be great. For the six minutes from 3.27 p.m. to 3.33 p.m. the flow is 10.80 grammes per 100 c.c. per minute, and for four minutes after the left hand had been removed from the warm water and dried, it is 11.55 grammes per 100 c.c. per minute. A second immersion of the left hand in cold water brought down the flow in the right to 5.67 grammes per 100 c.c. per minute (over a period of six minutes), the change occurring at once.

The next experiment (XXVI) shows that the reflex vaso constriction can also be obtained quite distinctly when the hand whose blood flow is being

measured is itself immersed in fairly cold water and the contralateral hand is transferred from this cold water to still colder water.

Experiment XXVI.

3.09 p.m. Hands (M.C.) put in bath at 22.0°. 3,015 c.c. of water in each calorimeter.
3.21 Hands put into calorimeters, right into R, left into L.

TIME.	R	L	NOTES.	TIME.	R	L	NOTES.
3.20	21.93	21.94	Room 22.0°.	3.28	22.87	22.79	Room 21.9°.
3.22	22.04	22.07		3.30	23.14	23.06	
3.23	22.14	22.18		3.32	23.37	23.30	At 3.33 put left hand into cold water (at 6.7°)
3.24	22.28	22.29		3.33	23.49	23.42	
3.25	22.45	22.43					
3.26	22.59	22.56					
3.27	22.72	22.68					
TIME.	A	NOTES.	TIME.	A	NOTES.		
3.34	23.59	Room 22.0°.	3.57	25.31	At 3.57 dried left hand and wrapped it in a towel.		
3.35	23.65		3.58	25.42	Room 23.0°.		
3.36	23.70		3.59	25.57			
3.37	23.77	At 3.43 transferred left hand to warm water (at 45°).	4.00	25.71	Room 23.1°.		
3.38	23.83		4.02	26.01	At 4.02 removed towel from left hand.		
3.40	23.96	The warm water is now at 41.5°.	4.03	26.11	At 4.05 put left hand into cold water (at 9°).		
3.42	24.10		4.05	26.29	Room 22.3°.		
3.43	24.16	Room 21.4°.	4.06	26.39			
3.44	24.24		4.07	26.46			
3.45	24.30	The warm water is now at 40.7°.	4.08	26.50	Withdrew left hand from the cold water and dried it.		
3.46	24.37		4.09	26.53	At 4.14 took right hand out of calorimeter.		
3.47	24.43	At 3.53 withdrew left hand from the warm water for a few seconds while warm water is being added to bring up the temperature to 45°.	4.10	26.58	Temperature of L 23.57°.		
3.48	24.51		4.11	26.64	Room 22.8°.		
3.49	24.61		4.12	26.68			
3.50	24.72		4.13	26.76			
3.52	24.94		4.14	26.86			
3.53	25.04		4.19	26.81			
3.55	25.18		4.21	26.76			
3.56	25.26		4.31				

Volume of right hand, 490 c.c. Volume of left hand, 470 c.c. Pulse 93. Mouth temperature 36.7°. Rectal temperature, 37.05°.

The flow for the right hand for the first ten minutes of the experiment is 7.77, and for the left 7.46 grammes per 100 c.c. per minute. For nine minutes during immersion of the left hand in cold water, the flow in the right is reduced to 4.02 grammes per 100 c.c. per minute. The minute readings show that the change has scarcely begun in the first minute. The reaction, therefore, appears to be somewhat less prompt than when the hand whose blood flow is being measured is at a higher temperature (Experiment XXV). The same is true of the reaction to immersion of the left hand in warm water. For the first five minutes of the immersion the flow in the right hand is only slightly increased (to 4.78 grammes per 100 c.c. per minute) while for the

second five minutes it is increased to 7.39 grammes. The minute readings show that the change is rather an abrupt one, beginning about the fourth or fifth minute after the immersion of the left hand. Exposure of the left hand for a few seconds, while still wet, to evaporation in the air, cuts down the flow in the right hand to 5.04 grammes. When the left hand is removed from the warm water, dried and wrapped up, the flow in the right hand increases to 11.14 grammes. The minute readings show that the change has already begun before the end of the first minute, although it has not yet reached its maximum. Even the cooling of the left hand caused by removing the towel, diminishes the flow in the right to 7.59 grammes. On again immersing the left hand in cold water, the flow in the right is reduced to 3.88 grammes, the change, as before, taking quite a minute to reveal itself.

It is instructive to compare these results in the normal person with the results in certain of the clinical cases. In a case of progressive muscular atrophy in a woman 46 years of age, (Mrs. N., Table II), the contralateral vaso-motor reflex elicited by cold was very prompt and persistent. The flow in the left hand was diminished from 7.13 grammes to 3.70 grammes per 100 c.c. per minute during the immersion of the right hand in cold water (at 8°), the diminution persisting during the eight minutes of immersion. In this case the reaction to subsequent immersion of the contralateral hand in warm water (at 43°) was paradoxical, a further small diminution occurring to 3.37 grammes. This result was never obtained in any normal case or in any of the other clinical cases. The explanation is afforded by the statement of the patient that the warm water caused painful tingling of the immersed hand, an effect never observed with the temperature used in any other case. The continued contralateral vaso-constriction was, therefore, a pain and not a temperature effect.

In a case of Raynaud's disease (Experiment XXVII) in a girl 15 years old (M. H., Table II), immersion of the right hand in cold water instantly cut down the flow in the left from 6.67 to 2.97 grammes per 100 c.c. per minute, an exceedingly strong reflex vaso-motor effect. This diminution, however, was much more transient than normal, and gave way to an increase even while the right hand continued in the cold water. This agrees very well with the idea that an underlying factor in Raynaud's disease is instability of the vaso-motor adjustment. Since this was written a similar effect has been observed in another case of Raynaud's disease in a woman 28 years old.

Experiment XXVII.

M. H., aged 15. A well developed girl. A little before Christmas (nearly three months ago), she noticed on coming in one evening that the two distal phalanges of each finger (including the thumb) of the two hands were "dead," pale, cold and numb. The weather was not particularly cold and frost-bite could be excluded. Since then she has had frequent attacks, each lasting an hour or two, the fingers then returning to normal colour and feeling. On being questioned, she says her nails do not grow as fast as before. In the intervals of the attacks her fingers feel cold, so that she dislikes putting her hands into cold water, although previously she used to like it. She works in a sewing establishment and sometimes finds her fingers too numb to sew. Since the condition began in the fingers she often has itching in the nose and the tip of it gets cold. Toes normal. For some time, but not before the condition in the fingers was observed, she also

has had cramp like pains in the right lower leg. The radial pulse is of good size in both wrists. Pulse rate, 112. She was not suffering from an attack at the time of the experiment. Mouth temperature, 37.2. Height 5 ft. 3 in.

2.24½ p.m., Hands put into bath at 30.2°. 3,015 c.c. water in each calorimeter.
2.35½ Hands put into calorimeters, right into R, left into L.

TIME.	R	L	NOTES.	TIME.	R	L	NOTES.
2.34	29.52	29.46		2.42	29.68	29.65	
2.37	29.50	29.44		2.43	29.70	29.69	
2.38	29.51	29.49		2.45	29.74	29.73	Room 23.6
2.39	29.53	29.51		2.46	29.77	29.75	
2.40	29.59	29.56		2.47	29.79	29.75	
2.41	29.62	29.60	Room 23.6	2.48	29.79		

TIME.	L	NOTES.	TIME.	L	NOTES.
2.49	29.82	At 2.48 put right hand into cold water (10°).	3.00	30.18	Warm water now at 40.9°.
2.50	29.83		3.01	30.21	
2.51	29.84		3.02	30.25	
2.52	29.90	The cold water is now 11.5°. She says the hand feels colder than it would have done before the trouble came on, but it does not look blue or paler than an ordinary hand.	3.03	30.31	Room 23.6
			3.04	30.35	
			3.05	30.39	
			3.05		Dried right hand.
			3.06		Wrapped up right hand in warm towel.
2.53	29.93		3.07	30.43	
2.54	29.99		3.08	30.44	
2.55	30.03		3.09	30.47	Room 23.5°.
2.56	30.05	Room 23.5°.	3.10	30.52	
2.57	30.11		3.11	30.55	
2.58	30.14	At 2.58 right hand put into warm water (43.0°).	3.12	30.61	At 3.12 took left hand out of calorimeter.
2.59	30.14		3.13	-	Temp. of R, 29.52°.
			3.30	30.40	Temp. of R, 29.36°.

Volume of right hand, 365 c.c.; of left hand, 340 c.c.

On withdrawal of the hands from the water at the end of the experiment, the epidermis over the two distal phalanges is seen to have a macerated appearance not observed in the same degree in any other patient or normal person for an immersion of this duration. No other part of the hands shows this condition except the ball of the right thumb. She says this region does not become cold or numb. Is there here, however, an indication that the region of feeble circulation is going to spread?

In a case of early brachial neuritis (J. S., Table II), the same condition is seen although not so marked. Here the flow in the affected hand is diminished (for a period of four minutes) from 10.29 to 5.18 grammes per 100 c.c. per minute by immersion of the normal hand in cold water. In the next five minutes, however, the sound hand being still in the cold water, the flow increases to 8.16 grammes per 100 c.c. per minute. The flow is considerably greater in the affected hand (10.29 grammes) than in the normal hand (7.66 grammes) when both hands are at the same temperature, probably owing to partial paralysis of the vaso-constrictor fibres in the affected nerve.

In O. A. H. (Table II), another case of early brachial neuritis, with a history of trauma, the same condition was observed, the flow in the hand on the affected side being 8.79 grammes, and in the other only 6.98 grammes per 100 c.c. per minute.

In a case of long standing brachial neuritis (Mrs. M. C., Table II), where distinct atrophy and disuse of the right hand had occurred, the flow is smaller on the affected side (3.98 grammes) than on the sound side (5.70 grammes).

In the case of M. B. (Table II), which is probably a neuritis limited to certain fingers of the right hand, and induced by some injury in the course of the man's occupation as a carpenter, the same marked but transient reaction to immersion of the contralateral hand in cold water is seen, the flow falling from 13.89 grammes to 7.25 grammes per 100 c.c. per minute for a three minute period after immersion, but increasing again to 11.13 grammes per 100 c.c. per minute for the remaining six minutes of the immersion.

In a case of old standing hemiplegia, due to cerebral hæmorrhage, the "stroke" having occurred nine years ago (C., Table II), the vaso-motor reflex studied cannot be elicited in the paralyzed hand by immersion of the sound hand either in warm or cold water. (Experiment XXVIII).

Experiment XXVIII.

C., aged 57. Hemiplegia. Had a stroke nine years ago. Left side paralysed, face, arm and leg. Left hand is colder than right; very little power in it. Mouth temperature, 37.07°. Pulse (sitting) 96. Height, 5 ft. 4 in. Weight, 152 lbs.

12.45 p.m. Put hands into bath at 30.7°. 3.015 c.c. water in each calorimeter.

12.57 Put hands into calorimeters, right into R, left into L.

TIME.	R	L	NOTES.	TIME.	R	L	NOTES.
12.56	30.29	30.11		1.07	30.77	30.33	
12.58	30.28	30.10		1.08	30.81	30.36	
12.59	30.32	30.12		1.09	30.87	30.38	
1.00	30.38	30.14	Room 22.0°.	1.10	30.90	30.39	
1.01	30.43	30.17		1.11	30.97	30.42	
1.02	30.49	30.20		1.12	31.00	30.43	
1.03	30.56	30.23		1.13	31.07		At 1.13 put right hand into warm water at 43.2°.
1.04	30.62	30.26					
1.05	30.68	30.30					
1.06	30.71	30.31					
1.14		30.49		1.26		30.73	
1.15		30.51		1.27		30.74	
1.16		30.53	Room 22.4°.	1.28		30.76	
1.17		30.55		1.29		30.79	
1.18		30.58	The warm water is now at 41.9°.	1.30		30.80	
1.19		30.60					At 1.30 dried and wrapped up right hand.
1.20		30.61		1.31		30.81	
1.21		30.63		1.32		30.82	Collar seen to be somewhat wet.
1.22		30.64		1.33		30.84	
1.23		30.67	At 1.23 put right hand in cold water (at 11.7°)	1.34	30.83	30.85	At 1.34 took left hand out of calorimeter.
1.24		30.70		1.43	30.74	30.78	
1.25		30.71	Room 23.1°.				

Volume of right hand, 422 c.c.

Volume of left hand, 376 c.c.

For summary of calculated blood flows see Table II.

The flow, which is originally 4.67 grammes in the paralyzed hand as compared with 9.15 grammes in the normal hand, comes out at 4.31 grammes per 100 c.c. per minute, both for the period of immersion of the normal hand in cold, and for the period of its immersion in warm water. The slight diminution has probably nothing to do with the immersion of the contralateral hand but is merely the expression of the slow continuous decline in the flow, especially where the circulation is feeble, often witnessed toward the close of a long experiment, and due partly to the increasing

venous congestion of the hands, which are hanging vertically down, and partly to vaso-constriction by the long stay of the hand in the water of the calorimeter, which is, of course, at a somewhat lower temperature than the normal temperature of the epidermis.

The absence of the vaso-motor reaction in this case may be explained by the secondary changes in the blood vessels, including the terminations of the vaso-motor nerves, in the long-paralysed hand, although possible changes in the vaso-motor path in the cord, secondary to the degeneration in the antero-lateral column conditioned by the cerebral lesion, cannot be excluded. This constitutes an organic paralysis of the vaso-motor reflex studied. A functional and, of course, temporary paralysis of the reflex was observed in a case (C. C. Table II) (Experiment XXIX), where one hand was inflamed from an infection of the middle finger. The flow in the infected hand was 11.93 grammes, or allowing for the effused liquid and reckoning the flow for the actual amount of hand tissue normally present, 13.05 grammes per 100 c.c. per minute, while the sound hand had a flow of only 4.92 grammes. The vaso-motor reflex elicited in the inflamed hand from the sound one, whether by cold or by warm water, was very slight, although in the normal direction. Obviously, as an adjunct or a consequence of the inflammatory process, the vessels were held permanently dilated and able to respond but slightly to the reflex stimuli arising in the contralateral hand. There is scarcely any doubt that the flow in the sound hand was smaller than normal, being probably reduced by a reciprocal reflex vaso-constriction, perhaps in part a pain stimulation, originating in the inflamed hand.

Experiment XXIX.

C. C., teamster, aged 36. Middle finger of right hand infected. First noticed four days ago. The hand is considerably swollen and the pain is sufficient to hinder him from sleeping. Pulse (sitting) 116. Mouth temperature, 37.8°.

3.44½ pain. Put hands into bath at about 30°. Put 2,970 c.c. water into R, 3,030 c.c. into L.

3.54 Hands put into calorimeters, right into R, left into L, as usual.

TIME.	R	L	NOTES.	TIME	R	L	NOTES.
3.53	29.60	29.60		4.04	30.66	29.85	
3.59	30.08	29.68		4.05	30.79	29.90	
4.00	30.49	29.70		4.06	30.89	29.95	
4.01	30.31	29.73		4.07	31.00	30.02	
4.02	30.43	29.77	Room 23.9	4.08	31.10	30.05	Room 23.8.
4.03	30.55	29.81					At 4.08 put left hand in cold water (94°).
4.09	31.18			4.18	32.02		
4.10	31.27	Room 23.6.		4.19	32.11		
4.11	31.34			4.20	32.19		At 4.20 dried left hand and wrapped it in a warm towel.
4.12	31.44			4.21	32.27		
4.13	31.55			4.22	32.35		At 4.22 took right hand out of R.
4.14	31.65						Temperature of Lisnow 29.87
4.15	31.74	At 4.15 put left hand in warm water 43°.		4.27			
4.16	31.83			4.38	32.11		Room 21.5.
4.17	31.91	Room 23.6					

Volume of right hand 580 c.c., of left hand 500 c.c., Height 5ft. 11 in., Weight 165 lbs., For synopsis of calculations of blood flow, see Table II.

In a case of Graves' disease (B., Table II), (Experiment XXX), the large blood flow of 14.18 grammes per 100 c.c. per minute in the right hand was promptly reduced to 7.82 grammes by immersion of the left hand in cold water, and the reduction continued during the period of immersion.

Experiment XXX.

B. Mm. Of middle age, Graves' disease. A tumour can be seen and felt on the right side of the neck in the position of the thyroid lobe. There was a swelling also on the left side, but this has disappeared under treatment. He says he is much better than he was. Exophthalmos is still present. He had marked tachycardia, but the pulse rate is stated to be less now than it was. Certain nervous symptoms still present. His hands and surface generally feel warm, and he states that he is always too warm. Mouth temperature, 36.4°. Pulse, 100 (sitting), 116 (standing).

11.50 a.m. Hands put into bath at 30.9°. At 11.57 a.m. temperature of bath is 30.8°.
12.00 Hands put into calorimeters. 3.015 c.c. water in each.

TIME.	R	L	NOTES.	TIME.	R	L	NOTES.
11.59	28.68	28.59		12.10	29.62	29.42	
12.01	28.78	28.60	Room 21.0.	12.11	29.68	29.50	Room 21.3.
12.02	28.88	28.71		12.12	Put left hand into cold water at 10°, rising during immersion to 11°. He feels the cold so keenly that he can only keep the hand in the cold water intermittently. This was not seen with any other patient.		
12.03	28.97	28.81					
12.04	29.07	28.92					
12.05	29.18	29.00	Room 21.2				
12.07	29.32	29.16					
12.08	29.43	29.25					
12.09	29.52	29.34					
12.12½	29.75			12.21	30.41		
12.13	29.77			12.22	30.20		
12.14	29.81	Temperature of L, 29.53.		12.23	30.27	At 12.23 dried and wrapped up left hand.	
12.15	29.84			12.24	30.32		
12.16	29.88			12.25	30.40		
12.17	29.92			12.26	30.48		
12.18	29.97			12.27	30.54		
12.18½		Left hand put into warm water (42.2°).		12.28	30.59	At 12.28 took right hand out of calorimeter	
12.19½	30.04						
12.20	30.05	Room 22.4.					

Volume of right hand, 375 c.c.; of left hand, 355 c.c.

Height, 5 ft. 7½ in. Weight, 127 lbs.

At 12.17 p.m. R has cooled to 30.38° and L to 30.20°.

For summary of calculated blood flow, see Table II.

The copious circulation in B. is in sharp contrast to the feeble trickle in the hands of A., a case of "dead fingers" of the right hand, a condition allied to Raynaud's disease but unilateral and confined to three fingers. These two patients and the patient C. were all, for one or two hours before the observations, kept under the same temperature conditions in the office of my friend Dr. Peskind, to whom I am indebted for the opportunity of examining them, and therefore the differences found represent real differences in the hand circulation of the individuals and not merely differences accidentally present or artificially produced under the conditions of the experiment. The relative increase in the circulation of the right hand of A. when the left is immersed in warm water is very great, although the absolute increase is

small. This agrees with observations on other cases in which the hand circulation was feeble, for example S. H., (Table II), a case of pulmonary tuberculosis. Here the flow of 0.3 gramme per 100 c.c. per minute in the right hand was gradually increased to 2.9 grammes during and after immersion of the left hand in warm water. This fell to 2.0 grammes on subsequent immersion of the left hand in cold water. In M. G., (Table II), a case of chronic dyspepsia, warming the left hand caused the flow in the right to increase from 2.88 grammes to 3.96 grammes, which on cooling the left hand, was diminished to 3.52 grammes. In J. M. (Table II), a case of aortic aneurism, the relatively small flow of 3.96 grammes in the right hand was only reduced to 3.42 grammes by immersion of the left hand in cold water, to rise to 5.5 grammes on drying and wrapping up the left hand in a warm cloth. In B., on the other hand, and in the normal person M. C. (Table I), in both of whom the hand circulation is habitually copious, the application of warm water to the contralateral hand, although it markedly increases the flow when it has been previously diminished by the immersion of the contralateral hand in cold water, does not increase it materially beyond the original level. This is what might be expected. The more widely dilated the arterioles, the smaller is the possible range of an additional reflex vasodilation, the greater the possible range of a reflex vaso-constriction and *vice versa*. In one case, that of J. V. (Table II), a boy suffering from pulmonary tuberculosis, with a weak pulse and poor circulation in the hands, the contralateral reflex normally evoked by warmth was not obtained nor was any effect produced by immersion of the contralateral hand in cold water.

NOTE.—Paper III. of this series, "The influence of forced breathing on the blood flow in the hands" appeared in the *American Journal of Physiology*, 1911, XXVIII, 133. Paper IV, "The influence of oxygen inhalation on the circulation in a case of cyanosis" in the *Journal of Pharmacology and experimental Therapeutics*, 1911, II, 477. A paper containing additional results on clinical cases is to be found in *The Cleveland Medical Journal*, 1911, x, 385.

10

F.

Al.

TABLE I -NORMAL PERSONS

PAROXYSMAL TACHYCARDIA ACCOMPANIED BY THE VENTRICULAR FORM OF VENOUS PULSE.

By H. HUME TURNBULL.

(*Melbourne*).

ALTHOUGH the rapid heart action in the case here recorded had lasted apparently continuously for 5½ months, the term paroxysmal tachycardia is applied to the case for the following reasons :

1. The type of heart beat was definitely abnormal, as shown by the form of the venous pulse and by the electrocardiograms.
2. The heart slowed in a way which is characteristic of true paroxysmal tachycardia, *i.e.*, the rate fell suddenly from 150 to 88 beats per minute; whereas in simple rapid heart action from toxæmia or defective innervation the rate falls gradually.
3. Before the slow rate was established, short paroxysms occurred, which were of an exactly similar nature to those previously recorded in cases of undoubted paroxysmal tachycardia, showing abrupt onset and offset; and during these paroxysms the polygraphic curves were precisely similar to those obtained during the prolonged tachycardia. For these reasons the prolonged tachycardia is regarded merely as a long paroxysm.

The patient was a man aged 74, a retired medical practitioner, who had led an active life, and had always been very fond of athletics. He had always been a very healthy man, and had never suffered from any illness. About a year before the onset of the present illness, while cutting a hedge, he ruptured most of the fibres of his right biceps muscle; previously he had sustained a similar, though less severe, injury to one of his leg muscles. He had never noticed any symptoms which directed his attention to his heart, except an occasional thumping beat, which gave him no distress. At the end of January, 1910, he awoke one morning feeling very seedy in an indefinite way; he was not breathless and could get about, but felt very unwell. He consulted Dr. Ford Anderson, who found his heart to be beating very rapidly, and advised him to go to bed and stay there, advice which he at first disregarded; but at the end of three days increasing weakness and shortness of breath, especially on exertion, compelled him to lie up. He could recline in comfort and sleep well, but his breathing was not quite easy.

Rest in bed and treatment gave no relief and on May the 16th, 1910, his condition was as follows: when lying quietly in bed, respiration was easy and he seemed quite comfortable, but on any exertion, even on talking, he became a little breathless. The lips and the nose were especially cyanosed. The heart's dulness extended from the right sternal margin to the nipple line on the left side, and there was dulness to the right edge of the sternum, as high up as the sterno-clavicular articulation. The apex beat was not palpable, and the heart sounds were weak but clear. The lungs were emphysematous, but no other abnormalities were detected on examination; the liver was not demonstrably enlarged, and there was no sign of oedema. The walls of the radial and brachial arteries appeared slightly thickened to the palpating finger. Polygraphic curves showed a regular pulse of 150 per minute, the venous pulse being of the ventricular form (as in Fig. 3 and 4).

Tincture of digitalis was given in doses of 20 minims three times a day, but no change was noticed till May the 23rd, when the patient awoke feeling very weak and ill, though he was soon comfortable again. Tracings taken on that day showed a great change in the heart's action. The pulse was about 88 per minute and markedly irregular. The irregularity was apparently due to a mechanism, transitional between the paroxysmal type and normal type. Four days later, the pulse was mostly regular, and the auriculo-ventricular sequence was normal, being interrupted by several paroxysms (Fig. 1 and 2): the beats of these paroxysms were precisely similar to those of the long paroxysm present before treatment was begun. The onset and offset of one paroxysm are shown: it ended in an irregular period, of the transitional type, and later the normal rhythm was resumed.

During this regular normal period, an interesting feature is a wave occurring regularly after the *r* wave in the venous pulse, at a constant distance after the *c* wave. Taking the irregular period in Fig. 2 (taken on the same day), it is seen that the regular rhythm is interrupted by four small beats which appear at shorter intervals than do the normal beats, and each is accompanied in the venous pulse by two waves *c* and *r*, as in the paroxysmal curves. Careful measurement shows that the auricular rhythm, which was very nearly regular over the slow period, was disturbed by the occurrence of these premature beats, showing that the normal pacemaker was affected by them, and suggesting that the impulses giving rise to these contractions arose in some abnormal part of the auricle.

The slow rhythm present on May the 27th, was not maintained, and on the succeeding day only a very few short strips showed normal beats, while by the 30th, the original tachycardia was entirely re-established (Fig. 3). This tachycardia was continued in spite of a full course of tincture of aconite, and by the beginning of July the patient's condition had become much worse. The breathlessness had been steadily increasing and the breathing was now very much oppressed, while definite dyspnoic attacks occurred at times. On July 9th, a second course of digitalis was commenced,

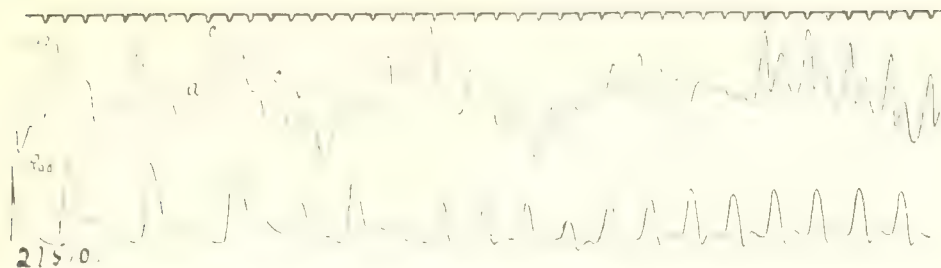


Fig. 1 *a* and *b*. Shows the beginning and end of the paroxysm recorded on May the 27th. The venous curve shows that the beats of the paroxysm are similar to those of the long-standing tachycardia.

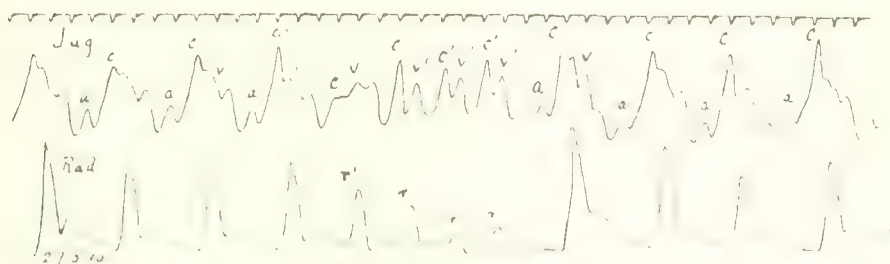


Fig. 2. The four shorter beats, marked *c*, show a venous curve similar to that of the paroxysm, and measurement shows that the auricular rhythm is upset by these beats, the interval between the preceding and following normal beats being more than three but less than four times the normal interval between beats. Note particularly the regularly occurring post-systolic wave.

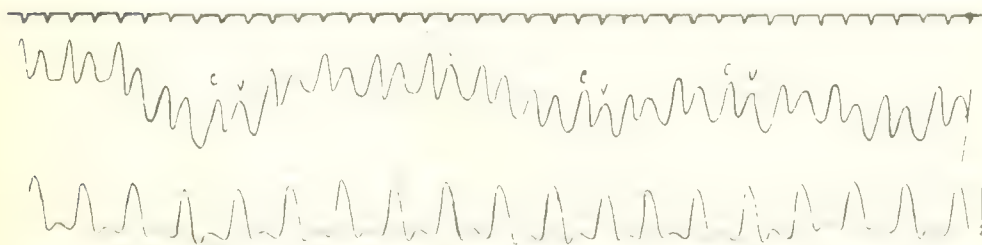


Fig. 3. May the 20th. Paroxysmal condition completely re-established; alternation less marked in the radial curve. (The same mechanism was present on the 16th and 24th.)

one of Nativelle's digitaline granules* being given three times a day. At this time the pulse rate was 150 per minute, and alternation was marked in the *radial pulse* (Fig. 4). On the evening of the 19th, he complained of nausea and loss of appetite and the digitalis was stopped, after he had taken 33 granules ($=8\frac{1}{4}$ drachms of tincture of digitalis).

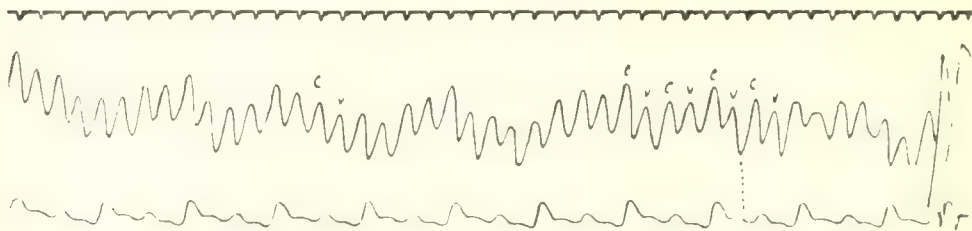


Fig 4. Condition on July the 15th, showing marked alteration in the radial pulse.

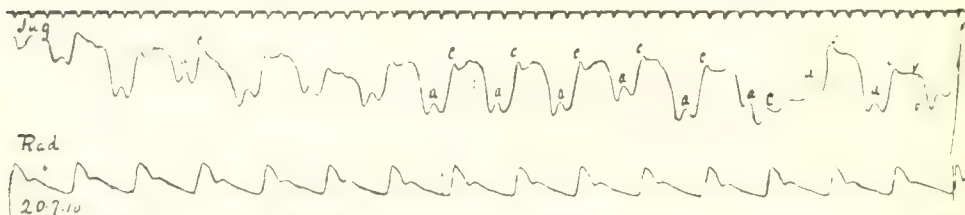


Fig. 5. Taken on July the 20th, during a regular period. The pulse rate is 76 per minute and the auricular wave is well marked in the venous curve.

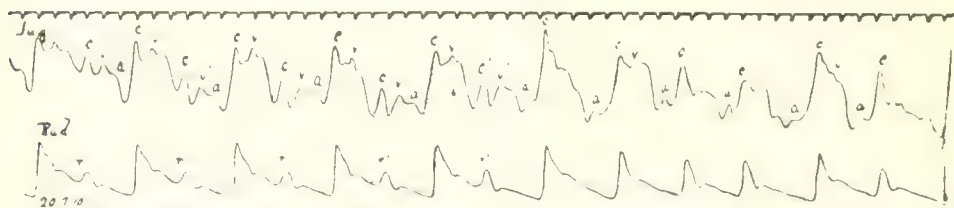


Fig. 6. Taken the same day (July the 20th); showing extrasystoles, which recur regularly over lengths of the tracing, and which are similar in the venous tracing to the beats of the paroxysm.

Tracings taken on the morning of the 20th showed periods of regular pulse at 76 beats per minute, with a normal venous curve, alternating with periods in which a small beat (r') occurred regularly between two large beats, the large one showing an a wave in the venous curve and the small one being an extrasystole of the same type as the beats of the main paroxysm (Fig. 5 and 6). On July 22nd, two days later, he complained of feeling very

* Dr. J. Mackenzie has shown that one of these granules is equivalent in effect to 15 minims of the tincture.

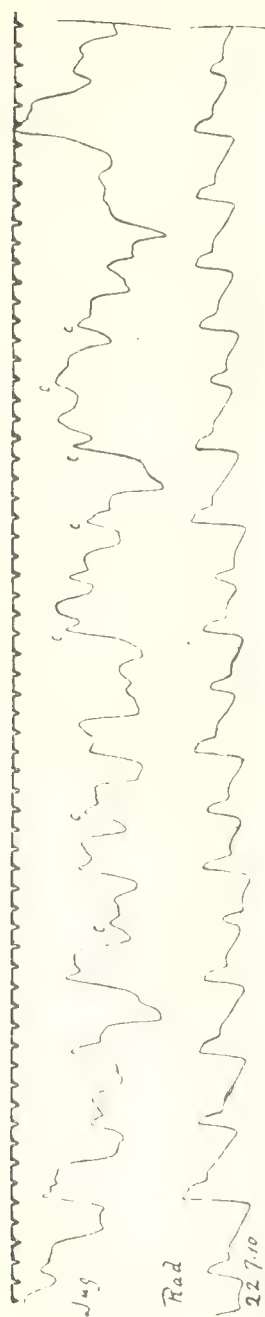


Fig. 7. The pulse is found, on careful measurement, to be completely irregular, and no wave corresponding to the auricular systole is to be found in the venous curves.

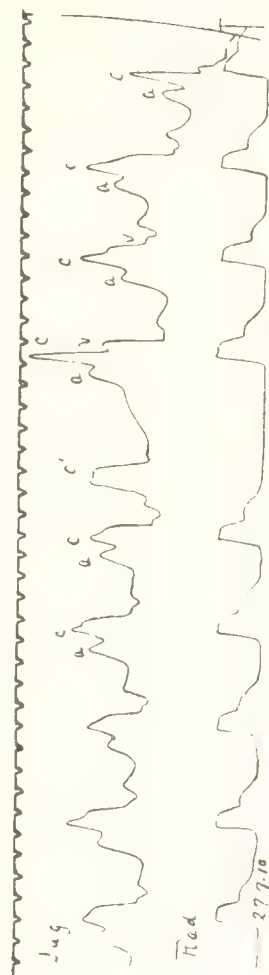


Fig. 8. Shows a pulse of 74 per minute. It is regular, except for an occasional extrasystole, the origin of which appears to be atrio-ventricular. (July, 1910).

unwell, the breathlessness being more marked than usual. He felt rather queer in the head and his memory was bad. He was restless and uneasy, talking a lot and rather wildly, and owing to his continual movements it was difficult to get a satisfactory tracing. A tracing was obtained however (Fig. 7), which showed a completely irregular pulse with no definite *a* wave in the jugular curve, though at times there was a single presystolic wave, and at others a series of waves through the diastole. There seems to be little doubt that the auricles at this time were in a state of fibrillation. On July the 24th, the pulse was perfectly regular, 72 beats per minute, and the venous curve showed normal regular *a* waves. There was still mental confusion and he felt rather ill and weak. From this time he was kept in bed, as it was thought that the movement entailed by getting up to dinner, as he had done previously, might re-induce the abnormal rhythm. On July the 27th he expressed himself as feeling very well, better than he had been for a long time. He was quite comfortable and could breathe with perfect ease, all traces of breathlessness had disappeared and his mind was now quite clear. The pulse was 72 per minute and quite regular, except for an occasional extrasystole, in which auricle and ventricle appeared to contract prematurely and so close together as to give rise to one large composite wave in the jugular pulse (Fig. 8).

From this time onwards, his progress was quite satisfactory, and after resting quietly in bed for about a week, he was able to get up again in the evening and shortly afterwards he went away for a change. He took things easily at first, but did more as his strength returned, and when last seen on November the 4th, he was very well and had just passed through a severe cold without distress and had completely recovered. He was able to walk about three miles each afternoon, half of it uphill, without breathlessness or the least distress. A tracing showed a pulse of 72 beats per minute, regular except for an occasional extrasystole the nature of which was uncertain; but as the period between the preceding and following normal beats was less than two pulse periods, the premature beat was probably auricular in origin.

Electrocardiograms showed a perfectly normal sequence of contraction.

Discussion of polygraphic curves.

The chief interest in this case centres around the nature of the two long paroxysms, one of which lasted so many months. During the attacks, the pulse was of the ventricular form. The heart mechanisms, which may be credited with the production of regular paroxysms of tachycardia in which no definite signs of auricular contraction are shown by the phlebogram, are several. The paroxysms may be of ventricular origin and may retrogress to the auricle, the paroxysms may arise in the junctional tissues, or they may arise in the auricle and be accompanied by an increased conduction interval. Each and all of these mechanisms may produce synchronous contraction of auricle and ventricle, and consequent masking of the

auricular waves. A fourth possibility is an auricular paroxysm with regular sequence of chamber contraction, where the auricular systole is too feeble to produce an effect upon the venous volume. The polygraphic evidence will not allow a final decision to be made between these alternatives, but the nature of the short paroxysms suggests that one of those which locates the origin of the tachycardia in the auricle is the correct interpretation.

In conclusion I wish to express my thanks to Dr. Ford Anderson and Dr. Mackenzie for the opportunity of examining this case; and to Dr. Mackenzie and Dr. Lewis for help in interpreting the curves.

Report on the electrocardiographic curves.

*By Dr. Th. Lewis.**

Two series of curves were obtained, one on May the 10th, 1910, during the long paroxysmal period; the other on November the 16th, 1910, when the sequence was normal. The two sets of curves are shown in a single figure, and it is to be observed that the rates, at which the films travelled, varied, (Fig. 9, *I*, *II* and *III* paroxysmal; Fig. 9, *IV*, *V* and *VI*, regular sequence). The interpretation of the paroxysmal curves was not possible until the later curves were obtained; and this fact emphasises the importance of obtaining the complete series in any individual case. The two series may be compared. Fig. 9, *I* and *IV* are from the same lead, namely right arm and left leg. The slow curve (Fig. 9, *IV*) enables the clear identification of *R* and *S* in the paroxysmal curve (Fig. 9, *I*). Fig. 9, *II* and *V* are leads from right arm and left arm. The slow curve gives the clue to *Q*, *R*, *S* and *T* summits in the paroxysmal curve. Fig. 9, *III* and *VI* are from left arm and left leg. The summits *R* and *S* are readily distinguished during the paroxysm.

The striking resemblance between the initial phases of the ventricular complex of paroxysmal and of post-paroxysmal or slow curves, in each of the three leads, is sufficient to identify the paroxysm as one of supraventricular origin. That is to say, it arises in a portion of the heart musculature constituted by auricle, auriculo-ventricular node and bundle. The exact relationship of the auricle to the paroxysm is not clear, but several conclusions are possible. Fibrillation of the auricle is excluded; none of the characteristic oscillations are present in the curves. The regular action of the heart and the repetition of the same picture from cycle to cycle, shows a similar action from beat to beat and evidences the origin of the paroxysm from a single focus in the heart musculature. Difficulty arises in fixing the end of ventricular systole. From the polygraphic curve it appears to have a duration of $1\frac{1}{3}$ sec.. This distance brings the measurement to a

*Working under the tenure of a Beit Memorial Research Fellowship, at University College Hospital Medical School, London.

point approximately mid-way between lines 1 and 2, as they are marked in Fig. 9, *I*, *II* and *III* and at or near the end of the summit marked *T* in Fig. 9, *II*. The remaining portion of the cycle, the small double summit following *T* in this strip, is probably the representative of an anomalous auricular contraction, but it cannot be distinguished with certainty. The whole stretch of curve between lines 1 and 2 in the three strips is in fact obscure. Lastly, the curves as a whole are opposed to the view of a nodal origin of the paroxysm, for they do not resemble those in which there is further evidence for such an origin. They tend to support the view that the paroxysm originates in the auricle proper, and that it has arisen ectopically, that is to say at a point removed from the pacemaker, giving rise consequently to an auricular electric representative of anomalous form, and one which it is difficult or impossible to recognise in the complete curve at the present stage of our knowledge.

SUMMARY.

(1) A case of paroxysm of regular tachycardia is described, in which the venous pulse was ventricular in form. It was probably due to a dislocation of impulse formation in the auricle. An observed paroxysm lasted several months.

(2) Under the influence of digitalis, fibrillation appeared, and later the normal rhythm was resumed.

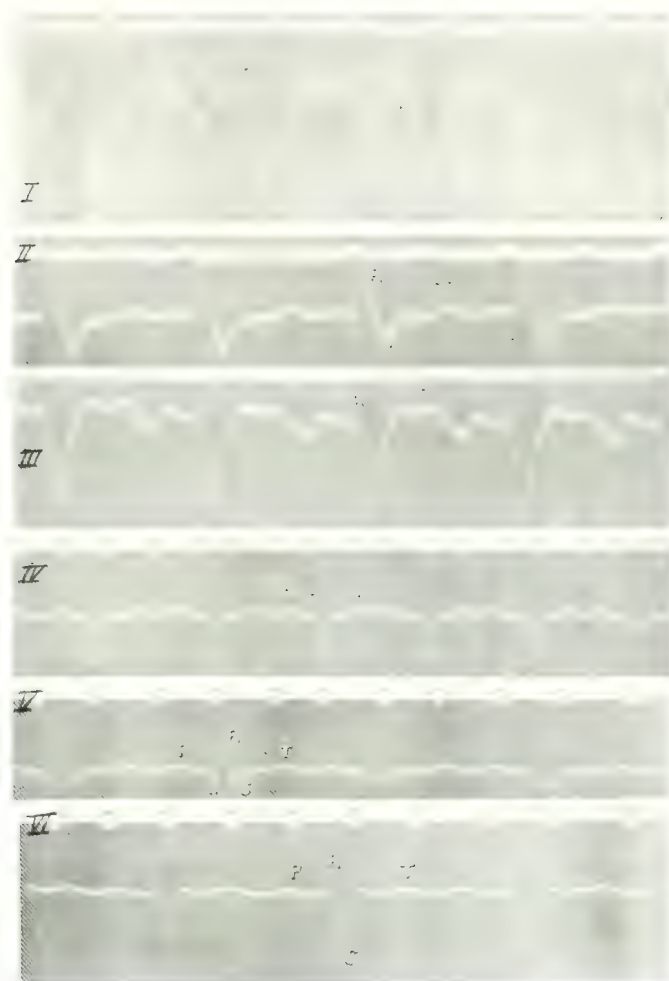


Fig. 9

HEART IRREGULARITIES, RESULTING FROM THE INHALATION OF LOW PERCENTAGES OF CHLOROFORM VAPOUR, AND THEIR RELATIONSHIP TO VENTRICULAR FIBRILLATION.

BY A. GOODMAN LEVY AND THOMAS LEWIS.*

(From University College Hospital Medical School).

Introduction.

THE following research was undertaken with a view to the further elucidation of certain cardiac phenomena, originally observed by one of us in connection with the administration of low percentages of chloroform to cats, and described in the form of a preliminary communication to the Physiological Society.⁴ In this paper a peculiar form of blood pressure curve was described, which is characterised by rapid heart action, high or medium blood pressure, and certain fluctuations and irregularities which are made evident by reason of the inertia of the mercury column in the Ludwig's manometer. This peculiar form of curve was found to occur quite commonly under chloroform administered at a lower percentage strength than 1 per cent., or thereabouts; and it is necessary to emphasise the point that it was obtained with great frequency in animals which had not had a large initial dose of the anæsthetic, and that it was not seen when the animals were under the full influence of the chloroform; it may be added, in confirmation of its frequent incidence, that it was readily obtained in the five experiments which form the basis of the present paper.

The significance of this irregularity was deduced from its uniform appearance immediately before the occurrence of heart failure as a result of fibrillation of the ventricles, a condition which was shown to occur in certain isolated instances in the course of a series of experiments carried out in another investigation upon cats under the influence of chloroform. Certain other irregularities, characterised by a regular intermission of the heart beat, were also frequently observed and appeared to be conditioned by the administration of a somewhat less rarified proportion of vapour.

It was further demonstrated that fibrillation of the ventricles could be induced in a large proportion of cases by the intravenous injection, under light chloroform anæsthesia, of small doses of adrenalin chloride, a drug which does not have a like effect under full chloroform anæsthesia or under any other ordinary experimental conditions; and that, when the cardiac

*Working under the tenure of a Beit Memorial Research Fellowship.

tracing was regular in the period preceding the injection, it assumed a form of irregularity before the onset of fibrillation, which was apparently similar to that described above as occurring spontaneously.

These observations appeared to us of sufficient importance to call for an investigation which would reveal the precise nature of the several heart mechanisms present under light chloroform anaesthesia.

Method.

Cats were employed exclusively. They were anaesthetised with chloroform regulated in percentage terms by means of an apparatus already fully described by one of us.⁵ A definite and known percentage of chloroform was conveyed by means of a Brodie's pump, through an elastic bag which served to convert the stream from an intermittent into a continuous one, to a funnel completely covering the face of the animal.

A blood pressure curve was taken on a kymograph drum, Hürthle's manometer being employed, with half saturated sodium sulphate solution in the connecting apparatus. Electrocardiographic curves were also obtained from time to time throughout the same experiments. The lead was in each instance from right shoulder to left groin. Two electromagnetic signals working in a single circuit (one writing upon the kymograph drum, the other upon the photographic paper) allowed simultaneous index marks to be recorded, and permitted the identification of the same beats in the Hürthle curve and electrocardiogram.

Intravenous injections of adrenalin chloride, as supplied by Parke, Davies & Co., were employed in the experiments. The dose administered was $\frac{1}{4}$ to 1 minim of the 1 in 1,000 commercial solution. (0.016 to 0.065 milligrammes), this being diluted with twenty times its bulk of normal saline solution previous to injection into the saphenous vein.

The irregularities produced by light chloroform anaesthesia alone.

The sole reference which we have found to irregularities of the heart, of the forms we describe and in experiments on chloroform, is in a paper by McWilliam.⁸ This writer incidentally mentions irregularities, which apparently correspond to the premature beats and bigeminal pulse which are fully discussed in the following paragraphs.

The irregularities of the heart, seen under light chloroform anaesthesia alone, were of varied form; a number of these will be described, and the description will be simplified if the irregularities observed in a single and typical experiment receive detailed attention. Emphasis should nevertheless be laid upon the fact that, from experiment to experiment, the types of irregularity encountered were very constant in form. Irregularity of the heart occurred when the tension of chloroform vapour in the inspired air

varied between .5 and 1.5 per cent. Repeated observation showed a definite relationship between the mechanism of the heart and the degree of anaesthesia. Thus, any animal which had inhaled 0.5 per cent. vapour for a few minutes, presented irregularity of the heart's action, and this was often marked in its degree. Similar irregularities were observed with higher percentages, for example 0.8 to 1 per cent., but as a general rule the degree of irregularity was less marked. Continued inhalation of percentages exceeding 1.5 per cent. usually abolished all irregularity. Short inhalations of 2 per cent. invariably abolished it.

The experiment chosen to exemplify the effects of chloroform upon the undamaged heart is illustrated by the electrocardiograms in Fig. 4. The animal was anaesthetised with 2 per cent. vapour, and during the succeeding ten minutes the strength was reduced in steps to 1 per cent.. The heart beat perfectly regularly on this percentage for five minutes, when the strength was reduced to 0.5 per cent.. A minute or so later the electrocardiogram and Hürthle curve showed marked irregularity. An electrocardiogram taken at this stage presented a tachycardia at the rate of 280 per minute and of the type seen in Fig. 4, *VI*; the actual curve is not published. The second electrocardiogram was taken approximately five minutes after the inhalation of 0.5 per cent. vapour commenced and is shown in Fig. 4, *I*. The curve demonstrates a regular bigeminy of the heart, due to premature contractions, such as are obtained on excitation of the apical or left portions of the ventricular musculature. The sequential beats are represented by the usual summits, *P*, *R* and *T*, and each cycle of this form is followed by an anomalous complex of which the first deviation is in the apex-negative, the second in the base negative direction. The sequential auricular contraction, (*P*) to which there is no ventricular response, falls with the anomalous complex and is readily identified in the curve.

The animal was next placed upon 1 per cent. vapour and after five minutes had elapsed, Fig. 4, *II* was obtained. The curve shows the regular occurrence of a premature ventricular contraction after each second normal or sequential cycle. It is to be noted that the type of anomalous ventricular complex has changed, but that it is still complicated by the sequential *P* summit which falls at or near its commencement. Fig. 4, *III* was obtained some five to six minutes later and subsequent to the reduction of the strength of vapour to 0.5 per cent.. The simultaneous Hürthle curve is shown in Fig. 1, and the corresponding beats in the two curves are numbered. A bigeminy is present in that part of the tracing covered by the signal marks, and it is brought about by premature ventricular contractions. The normal cycles (*P*, *R* and *T*) are followed by anomalous complexes and these are alternately of the types seen in Fig. 4, *I* and *II*.

A few minutes elapsed and the percentage was changed to 0.8 per cent.; a little later the heart showed a trigeminy (Fig. 4, *IV*). Premature contractions are shown in this figure after each second normal cycle. The corresponding ventricular complexes are of a third type, and consist of first

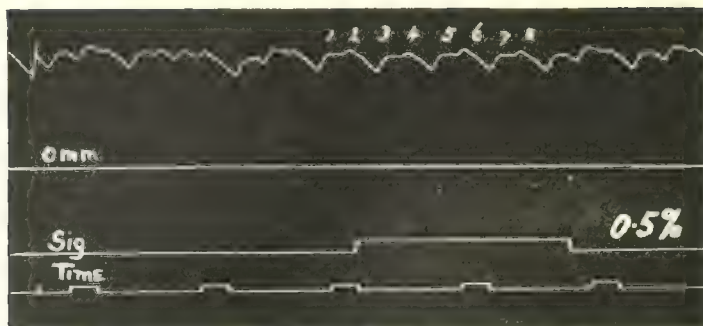


Fig. 1. A Hurthle manometer curve from the carotid of a cat under 0.5 per cent. chloroform vapour. The arterial curve shows an irregularity due to the presence of premature contractions. A portion of the curve, corresponding to the signal, has its beats numbered; the same beats are numbered in the simultaneous electrocardiogram shown in Fig. 4, III. The time is in 1.8 sec.

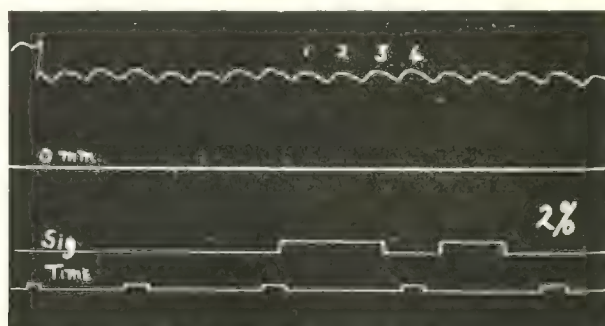


Fig. 2. A Hurthle manometer curve from the same animal, under 2 per cent. chloroform vapour. The arterial pulse curve is regular; the blood pressure has fallen. A portion of the curve corresponding to the signal has its beats numbered; the same beats are numbered in the simultaneous electrocardiogram shown in Fig. 4, V. The time is in 1.8 sec.

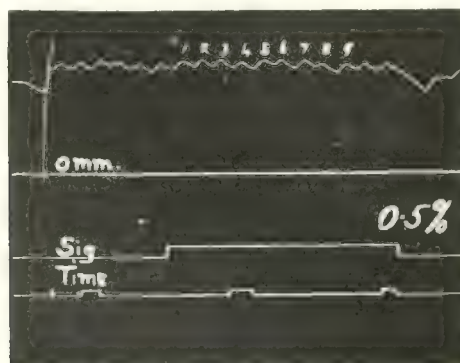


Fig. 3. A Hurthle manometer curve from the same animal, under 0.5 per cent. chloroform vapour. The arterial curve shows a number of rapid and almost regular beats, except towards the end where a pause occurs. Note the high blood pressure as compared to Fig. 2. A portion of the curve corresponding to the signal has its beats numbered; the same beats are numbered in the simultaneous electrocardiogram shown in Fig. 4, VI. The time is in 1.8 sec.

tall base-negative summits and secondly apex-negative summits; they conform in type to the anomalous complexes obtained upon stimulation of the basal or right portions of the ventricular musculature.

We need not concern ourselves with the accurate localisation of the origin of these beats; it is sufficient to emphasise the fact that each represents the origin of a ventricular contraction from a separate and fixed point or area, and that while in some curves the irregularity is due to new impulse formation from a single point or area (Fig. 4, *II*), in others two centres are active (Fig. 4, *III*).

The animal was placed upon 2 per cent. vapour and after the lapse of a few minutes the heart became perfectly and continuously regular. The mechanism is shown in Fig. 2 and 4, *V*, curves which were taken simultaneously. It is to be observed that the blood pressure had fallen somewhat with the rise in the percentage of vapour; the heart rate shown in the figure is 122 per minute. At the termination of this observation 0.5 per cent. was again administered and the simultaneous curves shown in Fig. 3 and 4, *VI* were obtained. The mechanism depicted in these figures, or a very similar mechanism, is extremely common upon the lighter percentages, and its analysis is aided by comparison with the other curves taken from the same animals. It consists of a rapid tachycardia of ventricular origin and is composed of beats which are placed at approximately regular intervals. The point of origin of the beats shown in Fig. 4, *VI* is variable and a comparison with Fig. 4, *I*, *II*, and *IV* shows that the new impulses are derived from areas which were previously active. Beats from three or more centres occur in haphazard sequence and follow each other at a rate of 232 per minute; no trace of auricular summits is to be found. It is probable that, with the establishment of the continuous tachycardia, the auricle is responding to ventricle and that the associated electric complexes approach the iso-electric state.

The Hürthle curve corresponding to this electrocardiogram is of peculiar interest, for it is, with the exception of the single long pause towards its termination, a regular and rapid pulse curve, in which the excursion of the several beats is approximately constant. Certainly the slight fluctuations seen are exaggerated when recorded by the mercury manometer, but the tracing as it appears in Fig. 3 might be readily mistaken, in the absence of other evidence, for that of a rapid and regular heart action of normal origin. The electrocardiogram, however, reveals the true nature of the condition; no single beat of sinus origin is present, but the mechanism is constituted by an ectopic rhythm generated in a number of ventricular foci. The importance of this conclusion is more evident when it is remembered that no *a priori* conclusions can be drawn in regard to the innervation of these new centres of impulse production. The approximate regularity of the tachycardia seems to be due to the appearance of a new contraction almost immediately at the cessation of the refractory period of the contraction which precedes it

Transitions between the simpler forms of irregularity shown in Fig. 4, *I-I V* and the tachycardia of Fig. 4, *VI* are common, and a single example which is taken from a separate experiment is shown in Fig. 5, the corresponding Hürthle curves as before being approximately regular. The auricular representatives are easily distinguished throughout the whole of this strip, but only a solitary normal cycle (*P*, *R* and *T*) is present. The premature contractions are coming from a number of separate ventricular foci.

A very curious type of tachycardia has been seen on several occasions and is illustrated by Fig. 6. It is a perfectly regular tachycardia generated from two separate ventricular foci, and the beats from one and the other focus occur alternately and follow each other at a rate of 312 per minute. In the corresponding Hürthle curves, the presence of two types of beat is recognisable only upon the very closest examination. The ventricular complexes of the beats follow each other so rapidly that each appears to start before the completion of the preceding one, and as a result the quick opening phases, some of which are directed upwards and some of which are directed downwards, do not start from the same abscissa. The explanation of the absence of return of the string to the isoelectric position before the occurrence of each new contraction is not apparent.

The effect of small doses of adrenalin upon the heart under the influence of low tensions of chloroform vapour.

In the first instance, it will be convenient to describe the result of injecting adrenalin, when the cat is under the full influence of chloroform; the sequence of events is similar to that described in the following typical experiment. An animal was anaesthetised with chloroform of 2 per cent. strength, which was gradually reduced to 1.5 per cent.. Thirty-one minutes from the commencement of the experiment, the anaesthesia was well established at this percentage; a faint corneal reflex was present, and the heart beat regularly at a rate of 160 per minute; the mean blood pressure was low, namely, 63 mm. Hg.. Under these conditions, 0.065 milligrammes of adrenalin chloride were injected intravenously. Approximately twenty seconds after the injection irregularities commenced to show themselves in the electrocardiogram, the first premature beat being an accompaniment of the rise of blood pressure, which had at this point reached a height of 90 mm.. The premature ventricular contractions became more numerous as the pressure rose to 100 mm., and irregular mechanisms were encountered, which were similar to those previously described as occurring under the influence of light chloroform anaesthesia alone, (cp. Fig. 4, *I I*, and Fig. 5*). The

The similar mechanisms described by Kahn were obtained in dogs deeply anaesthetised by a mixture of chloroform and ether. (Communication by letter.)

blood pressure having reached a maximum of 120 mm., the heart, 64 seconds from the time of injection, settled down into a regular tachycardia from a single point, probably located in the left or apical portions of the ventricular musculature. One minute later, the blood pressure had fallen to 105 mm., and the heart was beating at a regular rate of 210 per minute, and its mechanism was normal.

When the animal is under low percentages of chloroform vapour, the injection of adrenalin is followed by results which are far more profound than those obtained in animals under the higher percentages. It may be that, when the injection is administered, the heart is presenting the irregularities commonly found under light anæsthesia, or it may be that it is beating regularly; but independently of its initial condition, and provided that the anæsthesia is light, the injection of 0.016 milligrammes or more of adrenalin chloride is followed by the appearance of multiple premature ventricular contractions, and finally the disorder of the mechanism culminates in fibrillation. This sequence of events is exemplified in the following description of the result of a second injection of adrenalin into the same animal, which was the subject of the experiment already recorded.

At the conclusion of the previous observation, the percentage was reduced to 0.5 per cent., and the injection of 0.065 milligrammes of adrenalin chloride was given fourteen minutes later. At the moment of injection the blood pressure was 130 mm. Hg., and the pulse rate 277 per minute, the mechanism of the heart beat being one of alternate beats generated in two separate ventricular foci, and the curves being similar to those shown in Fig. 6. This mechanism continued for seventeen seconds, and at the end of this time, the blood pressure measured 145 mm.. The mechanism of the heart then suddenly changed to one in which beats from a number of foci followed each other at a rate of 230 per minute, and this continued for a period of two seconds, the blood pressure rising abruptly at the same time to 180 mm.. At the conclusion of this period, the ventricles fibrillated.

In another instance in which the same quantity of adrenalin was injected under 0.5 per cent. chloroform, the heart at first beat quite regularly at a rate of 120 per minute, it then passed suddenly into a condition of irregular tachycardia, generated in multiple ventricular foci. This lasted for seventeen seconds and terminated in ventricular fibrillation. The latter part of the tachycardia and its passage into fibrillation is shown in Fig. 7.

As a rule the onset of ventricular fibrillation terminates the experiment, for the ventricles fail to recover from it; but complete recovery from fibrillation lasting three seconds has been seen in one animal. From a number of kymograph tracings in our possession, it is obvious that permanent recovery from well established fibrillation is a rare event in the cat. In the above mentioned instance, a further injection under 0.5 per cent. vapour caused fibrillation, from which there was a temporary recovery, lasting some six seconds, the heart passing again into fibrillation, which, on this occasion, persisted.

When there is recovery from fibrillation, the mechanism at the offset is similar to that seen at the onset: tachycardias of the several forms described are present. The normal sequence is re-established with the administration of higher percentages of chloroform.

Briefly, the irregularities produced by adrenalin in small doses, when the animal is under *high* percentages of chloroform, are of the same nature as the irregularities produced by low percentages of chloroform alone: whilst small doses of adrenalin in the presence of low tensions of chloroform ultimately produce the highest grade of disorder, which is known to effect the ventricle, namely, fibrillation.

The electrocardiographic curve corresponding to ventricular fibrillation has been incidentally referred to by Kahn² and also by Jolly and Ritchie.¹ When the ventricle first passes into so-called fibrillation, its tone is increased, the visible movements are very active, and the oscillations are almost, but not quite, regular at a rate of 400 to 800 per minute. During this stage, a series of conspicuous and slow undulations usually occurs in the record, and this is well seen in Fig. 8. The curve as a whole shows a waxing and waning in the excursion of the oscillations at a rate of about 50-60 cycles per minute. The slow undulations are apparently associated with waves of tone change in the muscle, probably similar to the peristaltic waves spoken of by McWilliam.⁷ This stage of fibrillation, from which recovery is evidently possible in the cat, gradually gives place to a second condition in which the ventricle becomes more distended and in which the slow undulations are absent or inconspicuous, and in which the rapid oscillations occur at a slower rate (300-360 per minute) and in a far more irregular fashion. This mechanism, from which recovery has not been observed, is shown in Fig. 9. Similar appearances were seen by one of us in a series of experiments upon obstruction of the coronary arteries, experiments which frequently terminate in ventricular fibrillation, and similar changes have been noted also where fibrillation has been induced by faradic stimulation. The change from one type of fibrillation curve to the other, therefore, is not confined to experiments under chloroform and adrenalin: further, by whichever of these means fibrillation is induced, it is preceded by tachycardia of ventricular origin.

DISCUSSION.

The hearts of cats, influenced by low tensions of chloroform vapour alone, or by adrenalin in the presence of high percentages of chloroform, exhibit disorders of mechanism of a very definite type. So far as our observations are concerned, the disturbances result purely from the production of new impulses in the ventricles. The nature of these impulses has been fully discussed by one of us in a recent publication,⁶ and the beats have been termed *heterogenetic* on account of the short pauses which precede them and because they do not appear to stand as essential integers in a rhythmic

series of beats. Interpreting the events, in the light of the hypothesis put forward, we may state that the irregularities resulting from chloroform administration, are the outcome of an ever increasing tendency towards the production of heterogenetic beats : at first isolated and generated from a single foci, these beats subsequently become more numerous, and arise from several foci ; eventually the rhythm of the ventricle is entirely dominated by impulses of this nature, and immediately prior to the onset of the final inco-ordination in the adrenalin experiments, a number of foci are active. Final fibrillation can only be regarded as a further step in the train of events ; it is believed that it results from the activity of a number of new foci of pathological or heterogenetic impulse formation, and that a grade of inco-ordination is produced in the ventricular musculature, such as precludes the output of blood from the organ and brings the circulation to a speedy standstill.

Chloroform in low percentages produces an enhanced irritability of the ventricle, a condition in which there is a widespread discharge of pathological impulses from the musculature, or a condition in which there is a tendency to such discharges. A further interference, such as is brought about by adrenalin injection, is followed by the highest grade of ventricular disorder, *i.e.* fibrillation, and death results. The method in which the adrenalin acts on hearts, whether, for instance, by directly affecting the heart muscle or indirectly through its pressor action, is not a matter which concerns the present investigation, and cannot be discussed here. It is apparent, however, from the foregoing considerations that the heart under low tensions of chloroform vapour may be in a condition which is the immediate antecedent of ventricular fibrillation. This is obviously a matter of important clinical interest in relation to the causation of sudden death under chloroform anæsthesia.

The experiments are also of interest in that they help to elucidate the pathology of ventricular fibrillation. They appear to confirm the supposition that this disorder of the musculature results from the generation of heterogenetic or pathological impulses from a number of foci in the chamber itself.

The tachycardias observed under low tension chloroform vapour are of importance : they are of purely ventricular origin, and cannot be ascribed to any central nervous disturbance. They illustrate the value of the electro-cardiographic method, for in the absence of records of this nature, the heart mechanism might be and probably has been mistaken for a normal or sequential one ; and the acceleration of heart rate might be readily ascribed to altered innervation. It is necessary to emphasise the danger of serious fallacy when conclusions are drawn from sudden accelerations or retardations of pulse rate as recorded by a mercurial or membrane manometer. Mechanical records of this kind fail to provide the experimenter with an analysis of the heart mechanism and the changes in rate are too often interpreted as the result of central nerve influences.

CONCLUSIONS.

1. Low tensions of chloroform vapour, administered to cats, produce high grades of irregularity of the heart. The irregularities are due to the production of new impulses in the ventricular musculature.

2. Small intravenous injections of adrenalin chloride produce, under high percentages of chloroform vapour, a condition of irritability in the ventricle, which is similar to that observed to result from low percentages of chloroform alone.

3. Low tensions of chloroform administered to cats together with small intravenous injections of adrenalin chloride ultimately produce the highest grade of ventricular disorder, *i.e.*, ventricular fibrillation.

4. Ventricular fibrillation is the result of the origin of impulses at a number of separate foci in the ventricular musculature.

5. The irregular and rapid heart beat referred to in the introduction of this paper as a common accompaniment of the administration of low percentages of chloroform, and as a precursor of isolated instances of death from ventricular fibrillation in cats, is in fact a transitional stage towards ventricular fibrillation.

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FIG. 4.

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As a result of the above, the following theorem can be proved.

1. 5. 1971

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A CASE OF COMPLETE TRANSPOSITION OF THE VISCERA, ASSOCIATED WITH MITRAL STENOSIS; INCLUDING A DESCRIPTION OF THE ELECTROCARDIOGRAPHIC TRACINGS.

By SYDNEY A. OWEN.

(*From the City of London Hospital*).

COMPLETE transposition of the viscera is a very rare condition. Transposition associated with mitral stenosis is, so far as I am aware, a combination which has not been observed hitherto. Although no definite etiological factor can be traced, which can be held responsible for the mitral stenosis in this case, the combination of the two conditions is regarded as a matter of coincidence.

I am much indebted to Dr. Thomas Lewis who took the electrocardiographic tracings for me, and who has given me the benefit of his wide experience in their correct interpretation.

Clinical History.—The patient, an unmarried woman, aged 28, a tailoress, sought advice at the Victoria Park Hospital for cough without expectoration, shortness of breath and palpitation of fourteen days' duration. Beyond an occasional winter cough, she definitely asserts that she has never suffered in the past from any illness of sufficient gravity to make her seek medical advice. There is no history in childhood of rheumatism or any other acute specific illness. Her family history is without significance.

Present State.—She is an anæmic, though well nourished woman, whose aspect in other respects in no way indicates that she is the subject of well marked mitral stenosis. The heart's maximum apex beat is situated in the fifth *right* interspace, three inches from the mid-sternal line. There is a well marked apical presystolic thrill. Pulsation can be detected close to the left border of the sternum in the fourth and fifth intercostal spaces and, to a less extent, in the epigastrium. The veins at the root of the neck are not unduly prominent. There is no cyanosis or clubbing of the fingers. The radial pulse is small but regular in force and rhythm. The left border of the heart's dulness, as mapped out by moderate percussion, is situated a finger's breadth to the left of the left border of the sternum. The right third costal cartilage forms the upper border of this cardiac dulness. On auscultation at the apex, the first sound presents the classical characters

associated with mitral stenosis. In addition there is a well marked pre-systolic and a short systolic bruit with an imperfectly reduplicated second sound. At the pulmonary base of the (transposed) heart, the second sound is accentuated. The sounds are natural at the aortic base. From a consideration of the symptoms and physical signs, it would appear that the mitral stenotic lesion is of moderate grade and that the heart is undilated.

A liver dullness with normal limits can be mapped out on the left instead of on the right side. A normal stomach note can be elicited on the right side. The spleen cannot be felt, but is percussed on the right side. The urine is normal. Physical examination reveals no organic disease in the lungs, abdomen or central nervous system.

Electrocardiographic examination.

The electrocardiographic examination of patients who are the subject of complete transposition gives results which are readily anticipated, and of which this case serves as an illustration. The heart, its several chambers and vessels, is placed with precisely those relationships to the right side of the body which it usually bears to the left side of the body. Its long axis runs obliquely, from above and to the left, downwards and to the right.

The usual leads adopted by Einthoven for the normal subject are (*I*) from right arm (R.A.) to left arm (L.A.), (*II*) from right arm to left leg (L.L.), and (*III*) from left arm to left leg. The appropriate leads in the transposed subject are necessarily left arm to right arm, left arm to right leg, and right arm to right leg.

The appropriate leads (transposed leads) from the patient here considered are shown in Fig. 1, 2 and 3. Each demonstrates three summits, *P*, *R* and *T*, directed in the upward or base-negative direction.

Fig. 1 (L.A. to R.A.) shows a prominent *P* summit, as does also Fig. 2, the lead from L.A. to R.L., and in Fig. 3 (R.A. to R.L.), *P* shows a tendency to bifurcate; these are characters which are in accord with the remaining physical signs of mitral stenosis. Fig. 1 shows a small *Q* deviation; Fig. 3 shows an *S* dip. In Fig. 1 *R* is increased, in Fig. 3 *R* is diminished; appearances consistent with hypertrophy of the transposed right ventricle.

Transposition of the heart is readily diagnosed, and is diagnosed with certainty by means of the galvanometric examination. *The usual pictures are only obtained when the leads are transposed.* If the ordinary (non-transposed leads) are adopted, the presence of transposition is manifested by the appearance of the curves in lead *I* (R.A. to L.A.). The lead is a direct reversal of the appropriate lead (namely L.A. to R.A.); the curve is consequently upside down but otherwise unaltered. Transposition is not so evident in the curves obtained by leads *II* and *III*; the variations *P*, *R* and *T* are directed upwards in leads *II* and *III* in the transposed as in the normal subject. The reason for this is obvious. Lead *II* (R.A. to L.L.)



FIG. 1.

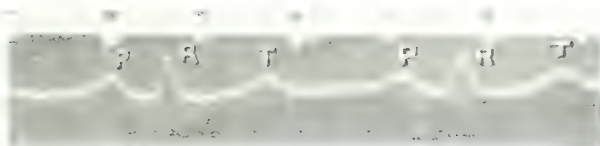


FIG. 2.

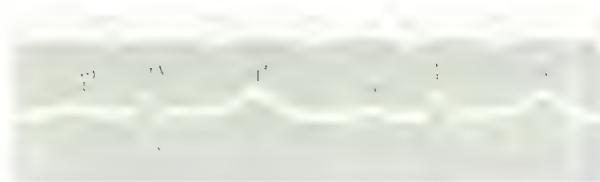


FIG. 3.

in the transposed subject gives practically the same curve as does lead *III* (L.A. to L.L.) in the normal subject ; for a lead from L.A. to L.L. gives a curve almost identical with L.A. to R.L. in one and the same patient ; the heart lies at some distance from the junction of leg to trunk and the utilisation of right or left leg alters the relationship of lead to lie of heart but little.

Similarly lead *III* (L.A. to L.L.) in the transposed subject yields a curve which is similar to that of lead *II* (R.A. to L.L.) in the normal subject, for the latter closely corresponds to a lead from R.A. to R.L..

The relationship of the curves obtained by means of several leads in the normal and transposed cases may be expressed in tabular form.

NORMAL SUBJECT.		TRANSPOSED SUBJECT.
R.A. to L.A. (lead <i>I</i>)	—	L.A. to R.A. (lead <i>I</i> transposed).
R.A. to L.L. (lead <i>II</i>).	— (approx.)	L.A. to L.L. (lead <i>III</i>).
L.A. to L.L. (lead <i>III</i>).	(approx.)	R.A. to L.L. (lead <i>II</i>).

In 1889, two cases of transposition were investigated by Waller,³ who came to the conclusion that the usual electric relationships are reversed in this condition. Quite recently Nicolai² has published diagrams of electrocardiograms from four cases, and Hoke¹ has added another example, from which he publishes an electrocardiogram. Nicolai² and Hoke¹ have shown that in leads from the right arm to left arm, the usual picture is completely inverted.

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VISCOSITY OF THE BLOOD.

By W. H. WELSH, M.D.

(*Edinburgh*).

CLINICAL WORK.

OBSERVATIONS upon the viscosity of the blood have been comparatively neglected in this country. A considerable amount of work has been carried out on the continent and is fully detailed in the medical records. Much of the work has been done with defibrinated blood in animals, while the clinical testing of the blood viscosity in man has been less undertaken, owing to the difficulty of keeping the unchanged blood fluid when drawn, and the lack of a suitable instrument for estimating the viscosity. For clinical work such an instrument must be portable, must be readily and quickly usable, must require only a small quantity of blood, and, most important of all, must possess means of maintaining a constant and known temperature and pressure. In these two last essentials many of the instruments fail. Those depending on a pressure-flask with mercurial manometer, or other such means of supplying pressure, are quite unsuited for any work outside the laboratory.

Most of those who have published work on viscosity have devised or modified a viscosimeter to suit themselves and named it accordingly. Of the various instruments, that devised by Determann⁸ best fulfils the above requirements, and is at present in use in the German Hospital, London. This viscosimeter has been tested in the laboratory against accurate physical instruments, and the results have been found to agree.

My own investigations on the viscosity of the blood have been made with Determann's⁸ instrument, and I give in this paper the results obtained in certain of my groups of cases ; but before going on to these I shall shortly discuss the nature of viscosity and the principle of the instruments used in estimating it.

All fluids possess the property of viscosity to a greater or less degree, and the study of the movement of fluids has been occupying the attention of physicists since early in the 19th Century.

As this property of fluids is well brought out by causing them to flow through capillary tubes, this method has generally been employed in estimating the viscosity.

It is known that a fluid, which wets the walls of a tube as it flows through it, moves forward in concentric layers. The outer layer next the walls of the tube is practically stationary, and the succeeding layers towards the centre, slide one on another, the central or axial stream moving most

rapidly. The resistance to its onflow is then due to the friction of the layers or particles of the fluid on one another, and is an internal friction. The outer friction or adhesion to the wall of the tube does not come into play to any appreciable extent after the walls are wetted by the fluid. It is to Poiseuille²² who in 1843 published results of his researches on the movement of liquids in tubes of small diameter, that we owe the sound basis upon which we now work. His experiments were very accurately carried out and they have since been proved by other investigators to hold good. He worked with capillary glass tubes of a diameter varying from .139-.632 mm., and these he used in a horizontal position. In his experiments he used defibrinated ox-blood, besides other fluids. He was the first to recognise the important influence of viscosity upon the circulation, and he considered it chiefly from the hæmodynamic point of view. Poiseuille²² worked out a formula by means of which the absolute co-efficient of viscosity of a liquid may be calculated from the quantity flowing through a tube of a certain length and diameter, under a certain pressure, and in unit of time. The lower the viscosity of the liquid the greater is the quantity; and the converse holds good. Poiseuille's²² formula is thus stated:—

$$Q = K \frac{HD^4}{L}$$

Q = quantity of liquid flowing out in unit of time.

H = pressure.

D = diameter of capillary.

L = length of capillary.

K represents the absolute co-efficient of viscosity for the liquid which is being tested and is a constant, only varying with the liquid employed, and the temperature. Its value is less the higher the viscosity of the liquid, and vice versa.

This, the original formula of Poiseuille,²² by which one obtains the actual co-efficient of any liquid, is not used in studying the viscosity of the blood. Instead, the simple method is employed of comparing the flow-through time of the blood with that of distilled water, which is taken as a standard. It is done in the following manner: the time of flow of a certain quantity of blood through a capillary tube, under a certain pressure, is compared with the time of flow of an equal quantity of distilled water, through the same capillary tube, under the same pressure and at the same temperature.

The flow-through time of the blood is divided by that of distilled water; and the result gives the relative co-efficient of viscosity for the blood.

When a glass capillary tube in the vertical position is used and gravity is the driving force, the flow through time of a certain quantity of distilled water is determined at a known temperature; then a similar quantity of

blood is allowed to flow through the same tube at the same temperature. As already shown, one has now merely to divide the time of flow through of the blood by that of distilled water, and the result gives a figure representing the relative co-efficient of viscosity of the blood.

The instrument used in the present work has been Determann's in its most recently modified form.

In using this instrument no artificially produced pressure is employed; the force of gravity is used instead. As to temperature, that of 20° C. is maintained during the experiment. To avoid variations in this temperature, a glass waterjacket surrounds the viscosimeter. This glass jacket is cylindrical in shape and tapers at both ends; it is about 8 inches in length and 2 inches in diameter. The opening at each end is closed by a small rubber-stopper through which the extremities of the capillary glass viscosimeter protrude. At the centre of the jacket, on the one side, is an opening with a rubber-stopper through which a thermometer is inserted and by which the temperature of the water is taken during the experiment; corresponding to this opening there is on the other side of the jacket a short attached glass rod, which with the projection of the thermometer, supports the jacket on its stand in a perpendicular position. The stand consists of two wooden up-rights on which the instrument, thus supported, can be easily inverted.

The viscosimeter itself consists of a glass capillary tube some 10 inches in length with two oval shaped dilatations or bulbs of equal capacity equidistant about $2\frac{1}{2}$ inches from the ends of the tube.

In using the instrument a rubber tube is slipped on to one end of the capillary, and the blood is sucked up by this means into the distal bulb of the viscosimeter to fill it exactly. It requires about .2 c.c. of blood. The instrument is then placed upon its stand and the blood allowed to flow through the capillary tube under the force of gravity.

The time of flow is taken exactly by means of a stop watch. The instrument is reversed and the process repeated, as in a sand glass. The blood is kept fluid by the addition of a small granule of hirudin placed on the skin before pricking and thus dissolved in the blood immediately it appears after the stab. The experiment does not require to be hurriedly carried out and the exact flow-through time of the blood can be determined. The first flow-through time is neglected as the glass walls must first be wetted by the blood; on the succeeding occasions the times are practically constant if the temperature remains constant. The time for distilled water has first to be determined by testing it in the particular instrument employed. As already noted, the time for the blood is divided by that of distilled water, and the result gives the relative co-efficient of viscosity of the blood. Previous to the use of the viscosimeter the glass jacket is filled with water at a temperature of 20° C. through the opening for the thermometer. If the temperature falls below this, it is easily raised by holding the instrument in the hands for a short time. The water must be kept mixed by moving the instrument to give a correct reading of the temperature.

Hirudin.

A great advance has been made in viscosity testing in its clinical aspect, with the discovery and preparation of hirudin in dry form.

Hirudin, or leech-extract, is a preparation obtained from the head of leeches. Haycraft¹³ was the first to discover (in 1884) the principle in the secretion of the leech's mouth which inhibited the coagulation of blood; while Franz¹¹ was the first to obtain the substance and prepare it in solution. It was injected into the vein in common salt solution, but in this form is not suited for viscosity-tests, as the addition of a watery solution alters the viscosity.

It is now prepared in dry form by Sachsse of Leipzig, and a minute granule (·00002 gramme) of this light substance is sufficient to keep 1 c.c. of blood fluid for a considerable time. Bodong and Caposi⁶ have shown (by experiment) that the hirudin does not in any way alter the physical properties of the blood, but only prevents coagulation. It is supposed to neutralise the thrombin or fibrin ferment, according to Morawitz.²⁰ Mellanby,¹⁹ who has been carrying out experiments lately, finds that hirudin contains both an anti-thrombokinase and an anti-ferment. Determann⁸ found that the addition of hirudin did not alter the viscosity of the blood, though Bence³ and others consider it necessary to use only a very small quantity, as it is apt to cause an agglutination and sedimentation of the corpuscles. Caposi⁶ stated that rouleaux formation was prevented, but this is not so.

I have been able to prove in a very satisfactory manner that the viscosity of the blood is not altered by the addition of hirudin. This was in a case of hamophilia, where the long coagulation time of the blood enabled me to carry out the experiment without hirudin. The result obtained was exactly the same as when using hirudin.

Viscosity 6·108 without hirudin.

Viscosity 6·108 with addition of hirudin.

Normal cases.

In order to have a standard for comparison, the first investigations were carried out in healthy individuals. Between sixty and seventy observations were made in these normal cases, of which about two-thirds were males and one-third females. These showed a wide range of variation in viscosity, from 4·74 to 6·02. Individual cases, however, showed very little variation as taken at various intervals.

The average in males worked out at 5·42.
 „ „ females „ „ 5·12.

The figures given by Determann⁸ are as follows:

The average in males, 4·798.
 „ „ females, 4·516.

Other writers who do not differentiate between males and females but give the average for all normal cases, are :—

Bence ⁷ (average)	5.4
Oswald ¹¹ ..	5.4.
Hirsch and Beck ¹⁵ (average)	5.1.
Hess ¹⁴ (average)	4.5.

I believe the figures in normal cases depend to some extent on the class of case investigated, whether hospital patients, in whom, of course, there is no illness to affect the condition of the blood, or healthy students and such as they. In men who have gone in for severe exercise, in the form of athletics for instance, I found a blood count, well over the figures cited as normal, generally 5,800,000 to 6,000,000 red cells per c.cm.. These cases of athletes also showed a high viscosity, about 5.8 on an average.

The blood count in healthy people is very frequently over 5 millions, and I consider that figure a low estimate of the normal red blood count.

Cyanosis.

I have grouped together cases showing well marked cyanosis from whatever cause, the greater proportion being due, however, to heart disease. These cases show exceedingly high values, much higher than any others which I have investigated. The case of Mrs. B., in whom the viscosity was 20.5, was one of mitral incompetence, with dilatation and venous stasis. A very high blood count, over 10 million, was also present. The degree of cyanosis was excessive. It required a deep stab to obtain the blood from the ear lobe, and the flow was slow, the blood appearing very thick and dark in colour.

The correctness of such high values as are given in the table below is disputed by Hess,¹⁴ who considers that the use of hirudin introduces error through sedimentation of the corpuscles, and more especially in cases where the viscosity is exceptionally high. I do not believe the hirudin to be the cause, for reasons stated in the last section and because the auto-agglutination of the corpuscles with separation of the plasma, which takes place in many bloods, occurs without the addition of hirudin: nor is it confined to blood of high viscosity, as in several cases where this phenomenon was well seen, the viscosity was low. The explanation is rather to be looked for in the fact that in these cases of cyanosis there is always a large increase in the number of the red corpuscles, and then the diameter of the capillary becomes a factor, the crowding corpuscles adhering together and tending to retard the flow through the tube of the viscosimeter.

Denning and Watson⁷ have given this explanation, but the experiments of du Bois Raymond, Brodie and Muller¹ go to prove that, in any case, this high viscosity as demonstrated in glass capillaries is of importance. They experimented with capillaries of the body and found that much the same differences occurred with an increased number of corpuscles, as occurred in the glass capillaries.

The increase of the carbonic acid content of the blood in these cases has to be taken into account. The effect of carbonic acid on the corpuscles

and on the viscosity has occupied the attention of several observers. The fact that the carbonic acid passed through the blood, alters the size and shape of the corpuscles, is known from the experiments of Haro and Ewald,⁹ Hamburger,¹² Koeppel,¹⁶ and others. The corpuscles are found to swell, losing their biconcave shape and becoming more globular, under the influence of CO₂. This is explained as follows:—When CO₂ is bubbled through the blood H₂CO₃ is formed. The carbonic acid attacks the alkali in the protein molecules and forms K₂CO₃ and water. More of this salt is formed in the corpuscles than in the plasma, because the corpuscles contain more alkali holding proteins. Consequently the osmotic pressure within the corpuscles is increased, water enters from the plasma, and the corpuscles swell. The interchange also results in a concentrating of the plasma, but the chief factor is the increased volume of the corpuscles. All observers seem to agree as to the increased viscosity in cases of cyanosis.

The following table outlines the viscosity values which I have obtained in cases showing cyanosis.

CASE.	AGE.	RED BLOOD CORPUSCLES.	WHITE BLOOD CORPUSCLES.	HAEMOGLOBIN.	VISCOSITY.	REMARKS.
Mrs. B.	f., 40	10,020,000	—	—	20.5	Mitral disease with oedema. Deeply cyanosed. Died a few days later.
Mrs. W.	f.	6,730,000	—	—	15.85	Mitral disease. Very ill. Extreme degree of cyanosis.
J. H.	m., 47	6,100,000	—	105%	7.67	Aneurism pressing on trachea. Well marked cyanosis.
E. H.	f., 9	6,300,000	11,000	110%	7.38	Congenital heart case. Cyanosis fairly well marked.
G. D.	m., 19	6,230,000	—	105%	6.27	Mitral valvular disease. Slight degree of cyanosis.
C. M.	m.	6,770,000	—	125%	8.23	Mitral disease; attacks of dyspnoea. Well marked cyanosis.
J. M.	m., 19	5,300,000	—	—	6.74	Mitral disease. Moderate degree of cyanosis.

Heart cases.

In the following list I give results obtained in cases exhibiting various valvular lesions of the heart, in which cyanosis was absent or was not a prominent feature. In some the heart lesions were slight and gave rise to few general symptoms; in others a certain degree of cyanosis and oedema was present. In themselves these heart lesions cannot be expected to alter the viscosity directly, but indirectly they may do so, in so far as they may cause an alteration in the blood, such as an increase in the CO₂ content, or in the number of the red cells. With one exception the heart cases showed raised viscosity values. Of the two cases, which showed no cyanosis, one had a somewhat increased and the other a lowered viscosity. In the case of the child with a congenital heart lesion, there was a systolic bruit in the pulmonary area with cyanosis and clubbing of the fingers. The blood pressure was low.

The mitral stenosis case showed a markedly irregular pulse, though the presystolic murmur and thrill were distinctly present.

Bachmann² stated that he obtained no striking difference in heart cases, compensated or otherwise. This is remarkable in view of the values

I have obtained. Unless, as I have already said, there is resulting cyanosis or polycythemia from the heart lesion, there can be no reason for an alteration in the viscosity of the blood.

Bachmann's² cases, where the viscosity remained normal while the patient was kept in bed, but became raised when the patient was allowed up, bear this out, as there would then be greater likelihood of dilatation and venous stasis.

The results of Determann's⁸ researches on viscosity in high climates are very important as regards heart cases. The great increase which he proves to take place in the viscosity of the blood at high altitudes, must of course be a source of danger in cases where there is heart weakness, because of the greater difficulty and increase of work experienced by the heart in driving the more viscous blood through the capillary circulation. There can be no question but that blood of high viscosity requires more driving power to force it through the capillaries than does blood of lower viscosity,* and that the dilating or contracting of the arterioles does not alter this fact, although it may partly compensate for it.

The fact that only a relatively small proportion of the capillary circulation is in use when the body is at rest, and that the remaining area can be called upon when necessary, as in cases of violent exercise, does not eliminate the effect of the higher viscosity, as the increased resistance due to it still comes into play in all this area of capillary network. It is difficult to estimate to what extent the variations of the viscosity affect the work of the heart where the blood flows in vessels of such varying calibre and tortuosity as obtain in the circulation of the body. Objection has been made to conclusions drawn from experiments made in rigid glass tubes. To a certain extent this objection holds good, as the conditions are necessarily very different *in vitro*; but as the glass walls are wetted with the blood in the same manner as are those in the living vessels, these experiments still indicate the amount of resistance due to the internal friction in the different bloods.

CASES.	AGE.	RED BLOOD CORPUSCLES.	WHITE BLOOD CORPUSCLES.	HAEMO- GLOBIN.	VIS- COSITY.	REMARKS.
M. H.	f., 18	5,200,000		80%	4.82	Pulmonary systolic bruit. This patient showed no symptoms of heart lesion.
E. H.	f., 9	6,300,000	11,000	110%	7.38	Congenital heart (S. B. P. 90). Slight clubbing of fingers. Confined to bed. Some degree of cyanosis.
G. D.	m., 19	6,230,000	—	105%	6.27	Mitral presystolic bruit; irregular pulse. Patient confined to bed. Cyanosis present.
J. R.		5,100,000	8,600	95%	6.37	Mitral incompetence; pulse irregular, slight oedema and cyanosis. Patient confined to bed.
J. M.	m., 19	5,300,000			6.74	Mitral incompetence; pulse irregular; some dilatation; moderate degree of cyanosis. In bed.
F. M.	m., 45	5,200,000			5.83	Double aortic bruit; heart enlarged and acting forcibly; pulse regular, large amplitude, typical "water hammer." Patient not greatly inconvenienced.

* The evidence for which statement receives further attention in the sequel.

Venesection.

In my researches on the means at our disposal of altering the viscosity of the blood in man by therapeutic measures, that of venesection stands out alone, as being the only certain method of obtaining a definite alteration. After drawing off some 10-12 ounces of blood from the arm, there is an almost immediate and very marked lowering of the viscosity.

I have no doubt that the beneficial effect of blood-letting, in cases of cyanosis and heart embarrassment, is greatly due to this lowering of the viscosity. The number of corpuscles is reduced also.

In the following list there is only one case which does not show a lowered viscosity after blood-letting, and that is the case of uræmic coma. But here there is an explanation in the fact that very little blood (4·5 ounces) was drawn off, as there was difficulty in getting the blood to flow. The patient was also much cyanosed and died a few hours later.

Burton Opitz⁵ showed the effect of venesection in animals, obtaining results which gave a lowering of the viscosity in every case.

He found, however, that the change was not proportional to the amount of blood drawn, nor to the changes in its specific gravity.

CASES.		RED BLOOD CORPUSCLES.	HÆMO- GLOBIN.	VIS- COSITY.	REMARKS.
M. M.	m.	6,770,000	120%	8·023	Mitral incompetence; some dilatation; slight oedema and irregular pulse. Marked cyanosis.
"		6,400,000	118%	7·232	Half-hour after bleeding (10 ounces).
F. B.	f.	4,250,000		5·14	Bright's disease (chronic).
"		—	—	4·14	After bleeding (14 ounces).
Mrs. N.		5,500,000		6·56	Eclampsia.
"		5,000,000		5·17	After delivery (with a good deal of hæmorrhage).
"		3,900,000		3·90	After venesection (11 ounces).
Mrs. M. L.		5,100,000	100%	5·81	Eclampsia.
"		—	—	5·23	15 minutes after bleeding (10 ounces).
"		—	70%	4·46	3 hours later.
M. B.		4,250,000	88%	5·16	Albuminurea and vomiting.
"		—	—	4·13	45 minutes after venesection (14 ounces).
"		—	—	3·27	2 days later.
T. M.	m.	6,500,000	106%	7·69	Uræmic coma. Difficulty in getting blood to flow. (5 ounces).
"		—	—	8·19	2 hours later and died.
W. W.	m.	6,360,000	105%	6·25	Hæmophilia.
"		—	—	6·21	Half-hour after venous puncture (2 ounces).

Bier's congestion.

The congestion of a limb by Bier's bandage causes an increase in the viscosity of the blood, as tested at a point distal to the bandage. It is only the blood in the limb, which is affected, as a control taken from the ear shows no alteration in the viscosity. When drawing off venous blood, the arm requires to be congested, and the varying degree of this congestion has probably an effect on the viscosity, the increase being more or less in accordance with the amount of congestion. The cause of the increased viscosity in the congested limb is probably the increased carbonic acid content of the

blood; in severe congestion a possible exudation of serum from the vessels and resultant concentration of the blood may also affect the results.

CASES.	VISCOSITY.	REMARKS.
J. W.	7.30	Blood taken from the toe.
	7.608	After 2½ hours slight congestion of leg.
W. W.	6.1	
	9.3	After 1 hour, severe congestion of arm.
J. A.	5.98	
„	6.30	After 1 hour congestion of arm.

Inhalation of oxygen in cyanosis.

Bence,³ giving oxygen by inhalation in cases of cyanosis, found a reduction in the viscosity, and a lowering of the blood-count. Those cases of cyanosis, due to heart insufficiency, reacted better than cases in which the cyanosis was due to disease affecting the respiratory system.

The case in which I made observations, was one of marked cyanosis from mitral disease, combined with polycythæmia. I found a slight lowering of the viscosity after the administration of oxygen, while the patient also showed some little improvement clinically, the breathing being less laboured and the cyanosis less marked. A complication in the form of chronic bronchitis was present and the oxygen was not inhaled very satisfactorily.

CASE.	AGE.	RED BLOOD CORPUSCLES.	VIS-COSITY.	REMARKS.
A. J.	m., 40	8,600,000	8.55	Oxygen given for 15 minutes three times during an hour.
		7,300,000	7.98	

In cases where the viscosity is very high, the experimental error comes into play to a greater degree. Any slight difference in temperature during the experiment causes a much greater variation in the flow through time in the case of a slow flowing viscous blood, than in a blood of low viscosity; again the capillary tube is not so well suited to test these bloods where the number of corpuscles is so great: the blood count, also, is by no means so accurate where the number of corpuscles is very high. In consideration of these facts, I do not hold this result to be of great importance. If oxygen inhalations improve the circulation in such a case, as they appear to do, the passage of fluid from the tissues into the vessels will naturally lower the viscosity of the blood.

With regard to medicinal agents I cannot say that I have found any that gave a constant or material alteration in the viscosity of the blood. In certain cases I administered calcium and citric acid in varying doses: and the general effect produced by the exhibition of these drugs was in the case of calcium to raise the viscosity, and in the case of citrates to lower it. The results however must be considered inconclusive, as their numbers have been insufficient.

Relation of viscosity to the coagulation of the blood.

I have estimated the viscosity and the coagulability in a number of cases, to determine whether, as has been stated, the one bears any relation to the other. The results show no relationship whatever. In taking the coagulation time I have used Addis's¹ method, warming the hand, and congesting the finger before pricking, to prevent any fallacy due to the blood not springing readily from the puncture. In most cases I have found little variation in the coagulation time from the normal, which is taken as about 8 to 9 minutes at 20° C.. The viscosity varied quite independently of the coagulability. The case of hæmophilia alone showed any great increase in the coagulation time. The maintenance of a constant temperature is essential if accurate results are to be obtained, in estimating the coagulability, as it is in estimating the viscosity. I have used the same temperature (20° C.) in both instances.

CASE.	VISCOSITY.	COAGN. TIME.	REMARKS.
W. W.	6.06	25 m.	Hæmophilia.
"	6.12	28 m.	"
"	5.86	32 m.	"
J. B.	5.20	9 m.	Jaundice.
J. H.	4.39	9½ m.	Purpura.
B. C.	3.78	4½ m.	"
A. S.	4.75	9 m.	Scurvy
P. A.	2.74	9 m.	Pernicious anæmia.
R. B.	7.0	7½ m.	Cellulitis of arm.
J. F.	5.90	7½ m.	"
"	4.90	6½ m.	" (6 days later).
D. S.	6.42	7½ m.	Typhoid fever.

Blood pressure and viscosity.

There does not appear to be any dependence of the blood pressure on the viscosity. It might be expected that an increased resistance in the capillary circulation due to increased viscosity would cause a high blood pressure. Other things being equal this must occur; but possibly the vasomotor control of the arterioles is more than sufficient to cope with any changes in the peripheral resistance due to the alterations in viscosity. Then again, in cases where the blood is very viscous, the heart's action may be embarrassed; and if the initial driving power supplied by the heart is low, there is no reason why the pressure should be high.

It is shown in the results given that in cases with a high viscosity the blood pressure may be low; and many of the cases with a high blood pressure show a low viscosity value. This last fact may be explained by there being hydræmia, with an increase in the total volume of fluid in the circulation.

In cases where the viscosity was reduced after venesection, the blood pressure was also lowered slightly in two cases, and was lowered enormously in another case which died shortly after the operation. In the case of

uræmic coma previously noted, where the viscosity rose after venesection, the blood pressure also rose.

CASES.	VISCOSITY.	BLOOD PRESSURE.	REMARKS.
A. B.	5.14	182 mm. Hg.	
"	4.14	178	After venesection.
M. B.	5.16	172	
"	4.13	178	After venesection.
"	3.27	190	12 days later.
Mrs. N.	6.56	216	
"	3.90	75	After venesection; died 1 hour later.
T. U.	7.69	218	
"	8.19	230	After venesection (5 ounces).
Mrs. D.	4.90	125	
W. H. W.	5.80	112	
E. H.	7.38	90	
Mrs. G.	6.10	190	

LABORATORY WORK.

I shall now give the results obtained in the laboratory, where I have experimented with larger quantities of blood. I obtained the blood from the median basilic or cephalic veins of the arm, by venous puncture with a large sized needle. In this way and having congested the arm, some 75 c.c. of blood could be easily drawn off. In some cases, in order to test the effect produced on the viscosity of the blood by passing carbonic acid and oxygen through it, I drew off the blood into glass vessels, lined with black paraffin and containing a solution of potassium oxalate. The oxalate solution was made up to 2 per cent., and by using a volume of this solution equal to one-tenth the quantity of blood, a .2 per cent. solution of oxalate was obtained.

In other cases I used hirudin in the dry form to prevent coagulation, instead of the oxalate. In this way there was no dilution of the blood, as is unavoidably the case with oxalate, and the viscosity of the unaltered venous blood could be obtained, also the viscosity of the undiluted plasma, after centrifugalisation. In the blood from a hæmophilic patient I was able to take the viscosity both of the capillary and venous blood, without the addition of hirudin; and comparing the results with those of the hirudinised blood, I proved that the viscosity is unaltered by the use of hirudin in the dry form.

I find that the viscosity of venous blood varies much more than does that of the capillary blood, which is a strong argument in favour of using capillary blood, in testing the viscosity. Venous has a constantly higher viscosity value than has capillary blood.

I also experimented with laked blood, finding a great increase in the viscosity from that of the same blood in its normal state. The significance of this I shall not discuss here.

Effect of passing carbonic acid gas and oxygen through the blood.

I carried out these experiments both with oxalated blood and with hirudinised blood, in two cases: one of them a healthy person, and the other a hæmophilic.

The blood was received in two separate glass vessels which were paraffined and charged with oxalate solution, or hirudin, as desired. One portion was then taken and, its viscosity having been determined, carbonic acid gas was bubbled through for several minutes; the viscosity was again determined and on each occasion showed a marked increase. The other portion was then similarly treated with oxygen in place of carbonic acid gas, and again the viscosity was increased, though in a very much less degree. This is contrary to the results which others give. I then passed oxygen through that portion of blood which had already been treated with carbonic acid gas, and found a distinct, though not great, lowering of the viscosity; but this failed to bring the value down to that of the blood treated with oxygen alone.

Finally I took the portion of blood which had been treated with oxygen alone, and through this passed carbonic acid gas. The viscosity was increased, not so greatly as in the case where the blood had not previously been treated with oxygen, but to almost the same value as that given by the portion which had been treated with carbonic acid gas first and then with oxygen.

These results, however, will show more clearly in tabulated form. The hamophilic case is shown in the first, the normal case in the second table.

DATE.	CASE.	RED BLOOD CORPUSCLES.	HAEMO-GLOBIN.	VISCOSITY.	REMARKS.
Mar. 6.	W. W.	6,200,000	103%	5.86	Capillary blood from ear lobe (hirudinised).
		—	—	6.7	Venous blood from arm (hirudinised).
		—	—	8.15	" " CO ₂ passed through.
Mar. 13.	W. W.	6,300,000	102%	6.50	Capillary blood from congested finger.
		—	—	6.82	Venous blood (no hirudin).
		—	—	7.28	" " (hirudinised) oxygen passed through.
		—	—	8.39	" " CO ₂
Mar. 20.	W. W.	6,400,000	103%	6.39	Capillary blood from uncongested finger.
		—	—	6.82	Venous blood from arm (no hirudin).
		—	—	7.54	" " with oxygen passed through
Apr. 10.	I. W. W.	6,400,000	104%	5.89	Venous blood oxalated.
	II.	—	—	6.06	" " after standing 16 hours.
	III.	—	—	6.84	" " oxygen passed through.
	IV.	—	—	7.23	" " CO ₂ " "

DATE.	No.	CASE.	RED BLOOD CORPUSCLES.	HAEMO-GLOBIN.	VISCOSITY.	REMARKS.
Mar. 20.	I.	T. A.	5,120,000	94%	5.08	Capillary blood from ear lobe (hirudinised).
	II.	—	—	—	5.16	Venous blood from arm (hirudinised).
	III.	—	—	—	5.36	" " oxygen passed through.
	IV.	—	—	—	5.82	" " CO ₂ " "
	V.	—	—	—	5.69	" " CO ₂ " " then oxygen.
	VI.	—	—	—	5.63	" " oxygen " " then CO ₂ .

In my experience the introduction of oxygen *in vitro* causes an increase in the viscosity. This is opposed to the results given by others. Bence³ quotes Koranyi, who using defibrinated blood, states that after saturating the blood with carbonic acid gas he passed oxygen through it and reduced the viscosity even below the original value for defibrinated blood. Rotky,²³ also, states that the passage of oxygen through the blood reduces its viscosity. It is not evident why it should do so, unless the oxygen is capable of driving off CO₂ by breaking up the H₂CO₃, in which form it circulates in the blood.

Only in the case of blood saturated with CO₂ did the oxygen affect a reduction in the viscosity: in the normal blood it did not do so, in fact it slightly raised the viscosity. The bubbling of the oxygen through the blood causes frothing, and probably increases rouleaux formation, which may account for this raised viscosity: and any oxygen dissolved in the plasma will tend to increase the viscosity, as does CO₂ when passed through serum or plasma (see below). The hæmoglobin in arterial blood, or blood which has been exposed to the air, is already saturated with oxygen and the passage of oxygen through it probably does not effect the volume or shape of the corpuscles.

The explanation of the action of CO₂ in raising the viscosity so markedly, is, according to Koeppe,¹⁶ as follows: the corpuscles, he states, contain more protein alkali than does the plasma, and so the carbonic acid acting on this alkali to form carbonates, there is a higher percentage found within the corpuscles. Osmotic action then takes place, the corpuscles taking up water from the plasma, and their volume becomes increased at the expense of the fluid in the plasma.

Viscosity of the serum and plasma, with results of passing carbonic acid gas through them.

The serum was obtained by allowing the blood to clot in a clean glass vessel; the plasma, by centrifugalising the hirudinised blood. The viscosity of the serum is slightly lower than that of the plasma; the absence of fibrinogen in the serum is probably the reason for this.

The viscosity of the serum is found to vary little and is of less importance than is that of the plasma. Burton Opitz,⁵ Mayer,¹⁸ Bence,³ Ferrai¹⁰ and others, give results of work done on serum. Burton Opitz⁵ worked at the effects of food, and Bence³ and Ferrai¹⁰ on those of CO₂. No marked alterations were found. The viscosity of the plasma does not vary to such an extent as to make it an important factor in influencing the viscosity of the whole blood. Kottmann¹⁷ gives the variations in all cases from 1.52 to 2.89.

The indirect influence of the plasma on the viscosity of the blood is of greater importance, as by its changing concentration, it causes shrivelling or swelling of the corpuscles (Hamburger¹²), thus affecting the viscosity of the blood.

The average viscosity for normal serum I find to be 1.74, while for plasma of hirudinised blood I get the value 2.06.

SERUM.	PLASMA.
1.71 before CO ₂ passed through.	2.043 before CO ₂ passed through.
1.73 after CO ₂ passed through.	2.065 after CO ₂ passed through.

In a case of hæmophilia, I estimated the viscosity of the plasma obtained by centrifugalising the blood, without the addition of any hirudin or oxalate, as coagulation was sufficiently delayed to allow of this. I give the viscosity of the plasma and of the serum.

Serum = 1.902. Plasma = 2.06.

The results already shown prove that the introduction of CO₂ into the whole blood greatly increases its viscosity; I have also just shown that carbonic acid introduced into the plasma causes only a very slight increase in its viscosity; it follows, therefore, that the increased viscosity of the whole blood is caused by changes in the corpuscles, and as the number of these cannot alter *in vitro*, it is to the increase in volume of the individual corpuscles that the raised viscosity is due. *In vivo*, besides these changes in the corpuscles, the increased number comes into play, as cases of cyanosis show a constantly high blood count.

CONCLUSIONS.

1. The viscosity of the blood varies little in health in the same individual but there is a range of variation in different individuals from 4.74 to 6.02.

2. The viscosity is higher in males than in females :—

Average in males	5.42
Average in females	5.12

3. The reason for the lower values in females would appear to be the lower blood count and hæmoglobin content found in these cases.

4. The number of the red blood corpuscles is the most important factor in causing variations of the viscosity. It varies also with the hæmoglobin content, but in neither instance does a strict relationship hold.

5. The carbonic acid content of the blood affects the viscosity, apart from an alteration in the number of corpuscles. This is shown *in vitro* where the corpuscles remain constant in number. The changes of viscosity are caused by alteration in volume and shape of the corpuscles, due to osmosis. Venous blood is of higher viscosity than arterial.

6. The plasma is of slightly higher viscosity than the serum and shows somewhat greater variations, though not in a degree calculated to markedly affect the viscosity of the whole blood.

Passing carbonic acid through the plasma causes but a very slight increase in its viscosity, a definite proof that the changes in the viscosity of the *whole blood*, when carbonic acid is passed through it, result from corpuscular changes.

7. The use of hirudin in the dry form does not effect the viscosity.

8. There is no relationship between the viscosity and the coagulability of the blood.

9. There is no fixed relationship between the viscosity and the blood pressure.

10. Venesection is the only therapeutic agent by means of which the viscosity can be certainly and definitely altered.

An immediate and marked lowering of the viscosity follows venesection, and this effect is not a transitory one.

11. In disease there are enormous variations in the viscosity of the blood : there is no disease which shows a constant variation from a normal value without corresponding changes in the corpuscles and hæmoglobin.

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OBSERVATIONS ON A CASE OF PAROXYSMAL TACHYCARDIA OF AURICULAR TYPE.

BY A. W. FALCONER AND G. M. DUNCAN.

(Aberdeen.)

J. M., a man aged 49, was admitted into the Aberdeen Royal Infirmary on August the 19th, 1910, under Dr. Edmond, to whom we are indebted for permission to observe the case. Although, unfortunately, electrocardiograms are wanting and polygraphic tracings were difficult to obtain on account of the marked dyspnoea and the mental condition of the patient, there can be no doubt that we are dealing with a case of paroxysmal tachycardia of auricular type, very similar to Mackenzie's case, exhaustively studied by Lewis,² and to Laslett's case.¹ Within the course of a week we find, at one time, the occurrence of isolated auricular extrasystoles, at another time, the presence of very short paroxysms of auricular tachycardia, and eventually the development of a similar paroxysm, which lasted three days.

Past history and habits. Until 7 years before admission to Hospital the patient had always been quite healthy. He denied ever having had rheumatic fever. Seven years before his present admission he was in the Aberdeen Infirmary with a form of venereal disease, details of which could not be obtained. He had not been a heavy drinker, and had smoked about 2 ozs. of tobacco a week. He was a carter by occupation, but he had not had unduly heavy labour.

Present affection. For fully 12 months before admission the patient had been troubled with increasing breathlessness on exertion, and occasional swelling of the feet and legs. He had remained at work, however, until a fortnight before admission to hospital, when he had to stop work as the breathlessness and swelling rapidly became much worse. He had not noted any palpitation, and had never lost consciousness. On admission the patient was found to be a well developed man. There was an old perforation of the palate, probably of syphilitic origin. There was marked orthopnea. There was a moderate œdema of the legs and feet with considerable swelling of the scrotum. The apex beat of the heart was situated in the 5th space $\frac{1}{2}$ -inch outside the nipple line. On auscultation double murmurs were heard at the aortic and mitral areas. The liver was somewhat enlarged and could be felt 1 inch below the costal margin. Free fluid could not be demonstrated in the abdomen. For the first few days the urine averaged rather over

30 ozs. a day, and contained a moderate amount of albumen. From August the 19th to the 23rd the pulse was about 100 a minute in rate, and was not noted to be irregular. No tracings were taken. During this time his general condition improved somewhat. On August the 23rd the patient's general condition was distinctly worse, and the pulse had become markedly irregular. On this date, a regular pulse rate of 100 a minute was frequently interrupted by a short series of rapid beats. Polygraphic records of this irregularity were obtained and will be described later. From August the 24th to the 29th the pulse was markedly irregular. For practically the whole of this time the irregularity consisted of 3 or 4 slow beats alternating with several rapid beats. This occurred with remarkable regularity. During this period the general condition of the patient became worse, the œdema and dyspnœa increased and he became extremely irritable and confused. Owing to the profound dyspnœa and mental irritability of the patient legible polygraphic tracings could not be obtained. On August the 29th the pulse rate suddenly rose to 185, and became quite regular. The condition of the patient remained much the same. This fast rhythm varied in rate from 185-150 per minute, and became gradually slower as the tachycardia continued. In the early hours of September the 1st the pulse rate suddenly fell to 100. The general condition of the patient was not much improved by the fall in rate. When examined on the morning of September the 1st the pulse was found to be perfectly regular at 100 a minute. Except for an occasional intermission, the regular rhythm continued until September the 8th, but the rate gradually rose from 100 to 120 a minute. The general condition did not improve, and the temperature which had previously been normal became irregular. On September the 9th there was a paroxysm of tachycardia lasting about 3 hours, and the patient died on September the 10th without any further paroxysms.

The polygraphic tracings.

Legible polygraphic tracings were obtained on August the 23rd, when the heart first became markedly irregular, and during the long paroxysm of tachycardia. Only radial tracings were obtained of the irregularity from August the 24th to the 29th.

Fig. 1 is a tracing obtained on August the 23rd. Following the 6th normal beat an auricular extrasystole without a full compensatory pause occurs. The beat is not transmitted to the radial. The *a* wave is combined with the preceding *c* wave, and has produced a large wave which has been deformed by striking the time-marker. The *a-c* interval throughout the tracing is rather less than one-fifth of a second. Fig. 2 shows a similar extrasystole, which is transmitted to the radial. The jugular tracing is unfortunately not good, but there can be little doubt that we are dealing with an auricular extrasystole. The pause in the radial in both is $\frac{1}{5}$ th of a second. Fig. 3 shows an auricular extrasystole in which the pause in the

radial is somewhat longer, namely, one second. The pause in the jugular tracing from a to a is $\frac{1}{5}$ th of a second, which is almost exactly equal to the post paroxysmal pause in Fig. 4. All the single extrasystoles obtained on this date corresponded to one or other of those two types. Fig. 4 is the only tracing of a paroxysm of tachycardia which was obtained on August the 23rd. It consists of 11 rapid beats and terminates in a pause which is also almost exactly equal to the pause following the auricular extrasystole in Fig. 3. With regard to the prolongation of the first beat following the paroxysm, a slow sinus rate with a gradual return to the normal, as a sequence

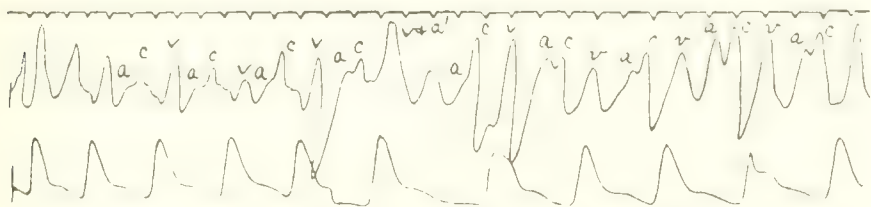


Fig. 1. Auricular extrasystole not conducted to the radial.

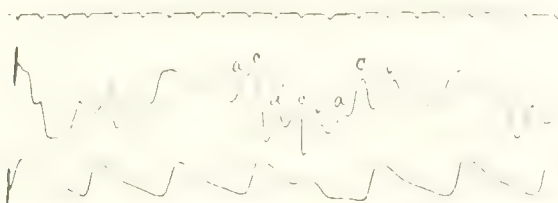


Fig. 2. Extrasystole similar to that shown in Fig. 1, but conducted to the radial.

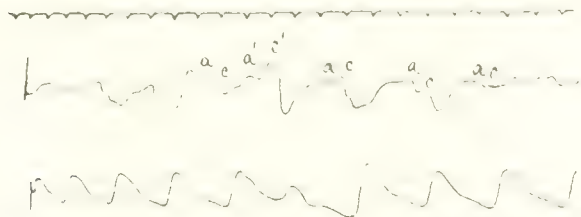


Fig. 3. Auricular extrasystole with somewhat larger pause than the extrasystoles in Figs. 1 and 2.

to a paroxysm, was a constant phenomenon in two cases observed by Lewis.² In Laslett's case,¹ as in the present one, the first normal pulse period was prolonged. Throughout the whole of the short paroxysm there are well marked a waves with an a - c interval of one-fifth of a second, that is to say, rather more than the a - c interval of the normal rhythm. The excessive height of the a waves during the paroxysm is partly due to the shortened V s-As interval, the a wave falling back on the preceding v wave, but it is possible that the four very large a waves in the middle of the paroxysm are

partly dependent on respiration. At the commencement of the paroxysm the first two beats of the radial curve differ somewhat from the succeeding nine beats. They lie somewhat lower in the curve, and do not raise the arterial pressure to the same extent as the following beats. In the jugular tracing the only discernible difference is that the $a-a$ interval between the first and second beats is distinctly less than the $a-a$ interval of the succeeding beats. This peculiar appearance of the radial tracing at the commencement of a paroxysm was an almost constant phenomenon in the numerous radial tracings of short paroxysms which were obtained from August the 24th to the 27th. That these are extrasystoles arising in the auricle there can be no doubt, but from polygraphic tracings alone, it is impossible to state definitely whether they differ from the later beats of the paroxysm. Lewis has carefully studied the onset of the paroxysms in his case and found that they were frequently introduced by one or more auricular extrasystoles which gave electro-cardiograms of different type from those of the paroxysm proper. He laid stress on the different appearance of those extrasystoles in the radial tracing, as a means of differentiating them from the beats of the paroxysm proper. Fig. 5 is an example of the rhythm which continued with remarkable regularity from August the 24th to the 29th. It bore no constant relation to respiration. As in Fig. 4, every short paroxysm is initiated by two small beats which differ somewhat from those of the rest of the paroxysm. The post-paroxysmal pause in the radial is quite constant in length, and is equal to the pause in Fig. 4. Fig. 6 is a tracing taken on August the 29th during the long paroxysm, when the pulse rate was 171, and shows that it was also of auricular origin with an $a-c$ interval of one-fifth of a second. On August the 30th alternation appeared in the radial tracing, and was more marked on the 31st. In the early morning of September the 1st the pulse suddenly fell to 100. Tracings were obtained some hours later, and showed a perfectly normal and regular rhythm of 100 a minute.

The nature of the paroxysms.

From a study of the tracings there can be no doubt that we are dealing with paroxysms originating in the auricle. As the $a-c$ interval is a full one-fifth of a second, we are justified in considering that the site of the stimulus is in the main mass of the auricular tissue.

Autopsy.

Permission to examine the chest and abdomen was obtained. The right pleural cavity was found to be obliterated by old adhesions, as also was the upper part of the left pleural cavity. The lower part of the left pleural cavity contained about 3 ozs. of clear serous fluid. The left lung weighed 2 lbs. 14 ozs.. There was marked emphysema of the upper lobe and the lower lobe was almost entirely solid. The right lung weighed 2 lbs.

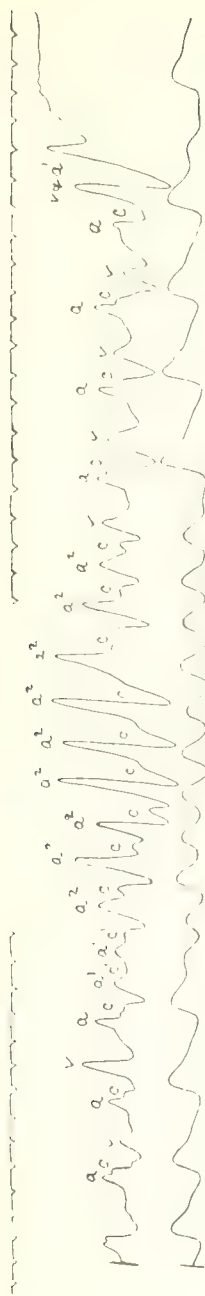


Fig. 4. Short paroxysm of auricular tachycardia.

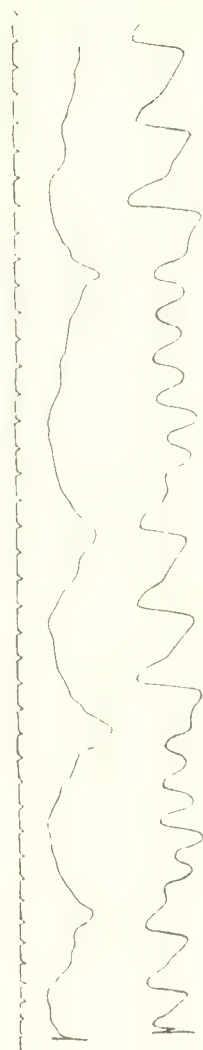


Fig. 5. Two short paroxysms of tachycardia. Lower tracing, radial; upper tracing, isopropyl.

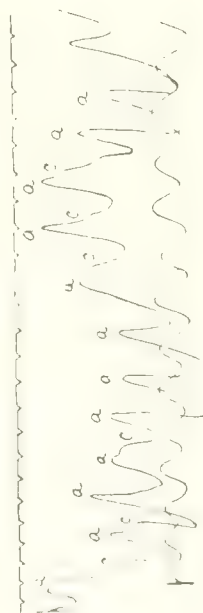


Fig. 6. Tracing of long paroxysm of tachycardia.

5 ozs. and was markedly oedematous and congested. In both lungs there was a marked irregular fibrosis. Microscopically both lungs showed a well marked irregular fibrosis which was probably syphilitic in origin. The left lower lobe showed all the features of a septic pneumonia. The liver was typically nutmeg in appearance. The peritoneal cavity was free from fluid. The left testicle was fibrosed.

The Heart. The pericardial sac contained 3 ozs. of slightly blood-stained fluid, otherwise the pericardium was healthy. The ascending and transverse arch of the aorta was somewhat dilated, and on section showed well marked aortitis which we believe to have been syphilitic. The heart itself was much enlarged. The walls of the transverse branch of the left coronary artery were very distinctly thickened. At its commencement there were some calcareous sclerotic patches but these only extended for a distance of about one inch. The interventricular branch of the left coronary artery showed much more extensive arterio-sclerotic changes. The wall was thickened and showed numerous calcareous areas, more especially in the upper part of its course. The lumen of both the transverse and the interventricular branches was dilated. The right coronary artery showed a moderate degree of thickening of its wall, but, except at its origin, the inner coat of the vessel showed no calcareous or atheromatous patches. The coronary veins were markedly distended with fluid blood, and stood out as cords the thickness of a large pencil. There was no evidence of any thrombosis. On opening the heart the aortic valves were found greatly thickened, nodular and contracted. They contained much calcareous deposit and they all showed irregular perforations. The cusps also showed numerous small warty vegetations of recent origin. The edges of the mitral valves showed a moderate amount of thickening. In the free margin, at the centre of the infundibular cusp of the tricuspid valve and projecting from the auricular aspect, was a small hard nodule the size of a pea. The surface was nodular and on section the nodule showed a patchy yellowish coloured surface of firm fibrous consistence, in which one or two small calcareous deposits could be felt. The left ventricle was greatly dilated and hypertrophied. After fixation in formaline the thickness of the wall varied from $\frac{1}{4}$ to 1 inch. To the naked eye, it showed no abnormality apart from the hypertrophy. The left auricle was slightly dilated and its wall was slightly thicker than normal. The right ventricle was not dilated. After hardening, the thickness of its wall varied from $\frac{1}{4}$ to $\frac{1}{8}$ of an inch. The right auricle was markedly dilated as was also the opening of the coronary sinus. In the upper postero-lateral aspect, near the site of the sino-auricular node, there was a dark fibrinous clot intimately adherent to the muscular trabeculæ. Below the opening of the interior vena cava, in the angle between the interauricular and right auriculo-ventricular groove, there were two irregularly shaped areas in which the wall of the auricle was of extreme thinness, presenting a semi-transparent parchment-like appearance. The

two patches lay parallel to each other and to the auriculo-ventricular groove. Elsewhere the wall of the auricle was of about the usual thickness.

Microscopic examination. Blocks containing the sino-auricular and the auriculo-ventricular node and the main bundle were cut in serial sections of 10 micra. The block containing the sino-auricular node included a considerable amount of auricular tissue and each third section was kept. Of the A-V node and bundle every tenth section was mounted. Sections were also cut from several other parts of the right auricle and from parts of the left auricle and right and left ventricles.

Right auricle. The wall of the right auricle showed throughout a definite fibrosis. Between the muscle fibres there was a diffuse small cell infiltration consisting for the most part of lymphocytes with scattered plasma cells and polymorphonuclear leucocytes; this infiltration was largely perivascular in its distribution. Many of the smaller arteries showed also distinct thickening of the inner coat. The muscle fibres frequently contained small perinuclear deposits of fine granular brown pigment, similar to those found in pigmentary involution of the heart. In those areas in which the fibrotic process was more advanced, granular and atrophied muscle fibres were occasionally seen.

The adherent clot in the upper part of the right auricle consisted of masses of fibrin and partially disintegrated red blood cells. The margin was extensively infiltrated with polymorphonuclear leucocytes, many of which were loaded with granular blood pigment. To a certain extent this leucocytic infiltration had affected the adjacent auricular wall.

Serial sections through the sino-auricular node and the auriculo-ventricular node and main bundle showed that these parts had not escaped the general lymphocytic infiltrations. The wall of the artery of the sino-auricular node was perhaps slightly thickened, but the lumen was not materially diminished. Several of the capillaries of this node showed well marked perivascular infiltration of lymphocytes, an example of which is seen in Fig. 7. Some of the lymphocytic deposits were not definitely perivascular (Fig. 8). The auriculo-ventricular node was well developed, and, in common with the main bundle presented small scattered lymphocytic deposits similar to those found in the sino-auricular node (Fig. 9).

Sections of the left auricle showed similar changes to those of the right auricle, but to a distinctly less degree. Sections of the right and left ventricles were normal, except for a very limited perivascular lymphocytosis and pigmentary involution.

SUMMARY.

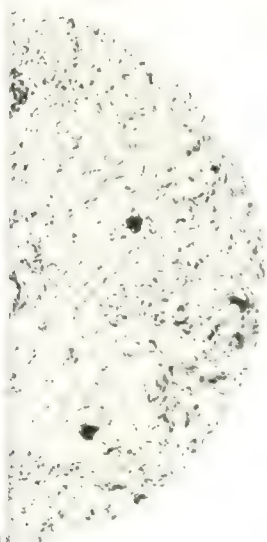
A case of paroxysmal tachycardia of auricular type is described. Post-mortem, in addition to various valvular lesions, extensive diffuse changes

were found in the tissues of the right auricle and to a less extent of the left auricle, which we interpret as of syphilitic origin. These had involved to a certain extent both the sino-auricular and auriculo-ventricular nodes. Except for a very moderate peri-vascular lymphocytosis the ventricular muscle was normal.

BIBLIOGRAPHY.

¹ LASLETT. *Quart. Jour. Med.*, 1911, IV, 295.

² LEWIS. *Heart*, 1910, 1, 306.



7. Small auricular node, showing marked perivascular lymphocytic infiltration of the main vessel.

7.

8. Small lymphocytic deposit in the periphery of the node.

9. Lymphocytic infiltration of the auricular node.

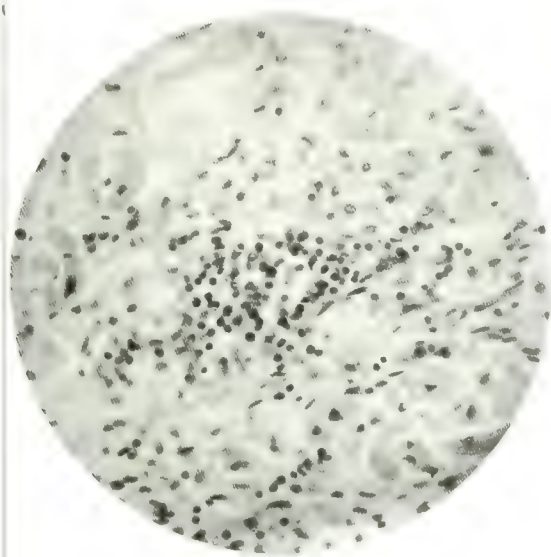


FIG. 9

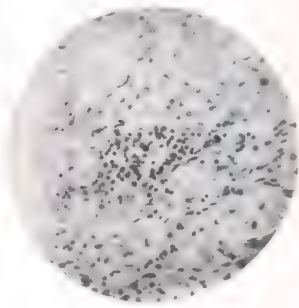
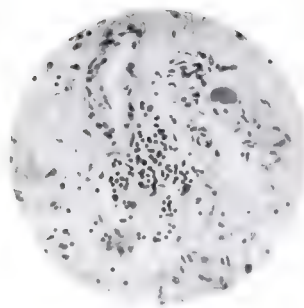
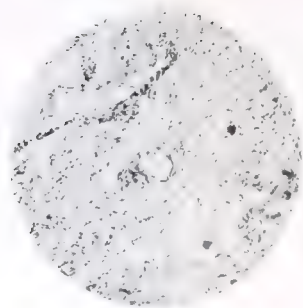


Fig. 8

Fig. 9

REMARKS ON TWO CASES OF HEART-BLOCK.

By T. WARDROP GRIFFITH.

(Leeds.)

IN placing on record these two cases of heart-block I desire among the points of interest which arise especially to emphasise four. These are, first, the difficulty which may exist in discriminating between a complete and a partial block ; secondly, the occurrence of complete block in a patient whose auriculo-ventricular conductivity had recently been shown to be normal ; thirdly, the occurrence of a peculiar auscultatory phenomenon, new to me and, so far as I am aware, unrecorded ; and fourthly the appearance of the *pulsus alternans* on some of the occasions when there was a certain numerical and time relationship between the auricular and ventricular beats and explicable on grounds which absolve one from attaching the usual grave prognostic significance to that occurrence.

CASE I. Mr. D., aged 71, had always had excellent health until about Easter, 1910, when he began to have pains in his shoulders followed by pains in his knees and hands. The knees became stiff and he went to Harrogate for treatment. There he was found to be the subject of suppurative alveolitis, and I understand that a culture was taken from the discharge and that a vaccine was prepared. Treatment with this was begun and in all six injections were given at intervals of ten days. The last injection was given on Monday, December the 19th at about 11 in the forenoon. Just before his midday meal he began to have peculiar feelings, which his subsequent experience showed were those which often preceded an attack, but it was not till afterwards that he noticed anything very marked. To the patient there was no suggestion of any cardiac condition, but the trouble seemed to begin in the head ; things in front of him became indistinct, there was a rushing feeling and then he appears to have lost consciousness. His medical man, Mr. H. J. Roper, saw him at about four o'clock in this first attack and when he was still unconscious ; at that time the pulse was infrequent and irregular, sometimes seeming to miss a beat and at others to stop altogether for a time. Between this hour and my first seeing him in consultation with Mr. Roper, which I did that same night at about 10.30, he had several attacks ; these were on the whole milder, but some of them were certainly attended with loss of consciousness. The pulse had remained irregular, sometimes seeming to stop, sometimes missing a beat and sometimes remaining infrequent for a time. Mr. Roper had to leave him for some little time before we met at his house. He was then very much better,

quite conscious and in no way distressed. His pulse was beating at 81, was quite regular during all the somewhat lengthy interview we had with him and was full and bounding. The tracing (Fig. 1) shows that the *a-c* interval was normal, being about one-fifth of a second. There was some arterial thickening, a little enlargement of the heart and a systolic bruit limited in distribution to the apex. On February the 13th, 1911, I again saw him with Mr. Roper. He had had many attacks with the same peculiarities in

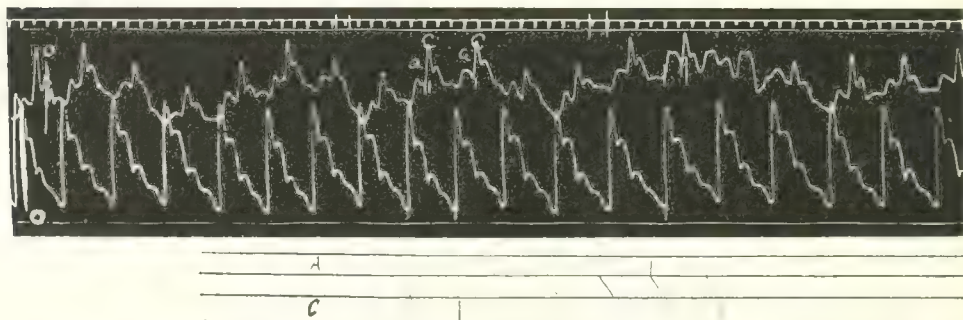


FIG. 1. Dec. 20th, 1910. Pulse 81. *a-c* interval about $\frac{1}{5}$. The ordinate of the time marker has been cut off.

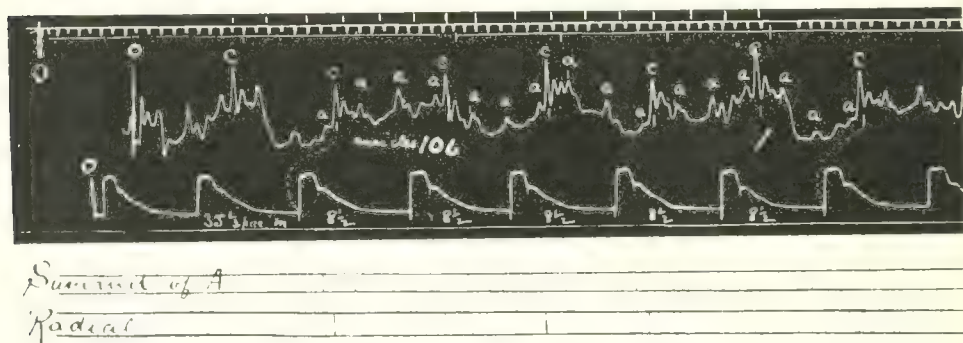


FIG. 2. Feb. 25th, 1911. P. 4, V. 15, 5

the pulse, which was infrequent in rate at the time Mr. Roper telephoned to me. On getting to the house, however, we found the pulse regular and beating at 79 and the *a-c* interval slightly shorter than before. On February the 23rd, Mr. Roper telephoned to me that the patient had been free from attacks for some days and that the pulse was then beating regularly at about 34 per minute. On February the 25th I took numerous tracings of his radial and jugular pulses and some of these are shown in Fig. 2, 3, 4 and 5.

In Fig. 2 the auricles are beating exactly three times as frequently as the ventricles: the distance from the summit of the *a* wave to the rise of the radial pulse (sometimes a convenient measurement to take) is very

nearly uniform, sometimes being one-fifth of a second and sometimes slightly less than that. Taking this tracing by itself few, I think, would fail to interpret it as an example of a partial block in which every third auricular stimulus passed from auricle to ventricle. The alternative view that the block is a complete one and that the strict multiple relationship of auricular to ventricular beats is purely fortuitous would probably not be entertained, but an examination of the other tracings, taken on the same day and within a few minutes of that shown in Fig. 2, indicate that this is really the case: for in all of these the block is clearly a complete one. In Fig. 3 the auricular rate is seen to be no longer a simple multiple of the ventricular rate and any interpretation based on the view that every third auricular stimulus gets through must carry with it the untenable conception of an *a-c* interval which progressively shortens until it vanishes. In the key printed under Fig. 3 it will be seen that the auricular systole marked 4 coincides in time with a ventricular systole and that as the auriculo-ventricular ratio is as 17 to 6 this event again happens with the 21st auricular systole. Fig. 4 and 5 do not require much explanation: each of them shows a condition of complete block with progressive shortening of the *a-c* interval which makes the alternative view almost untenable. Now all these tracings were taken within a few minutes of each other: I cannot say in what order they were taken, that shown in Fig. 2 may have been taken between two tracings both of which show the complete block: the patient maintained a uniform placid demeanour throughout and it would be hard to believe that the block was partial at one time and complete at another, though of course this is possible. I am therefore strongly inclined to think that in every case we have to deal with a block which is complete and that the simple multiple relationship which prevails in Fig. 2 must be accounted for by the long arm of coincidence. On March the 4th I again saw this patient and found the block still complete. One of my tracings showed that the auriculo-ventricular ratio was as $97\frac{1}{2}$ to 28 and another that it was as 92 to $26\frac{1}{2}$. I did not see him again. Mr. Roper tells me that the pulse remained infrequent, sometimes falling to 20 and on one occasion being noted at 18. I understand he had no further attacks but that he slowly went down hill and died with a failing left ventricle.

On both occasions when the block was complete, I noted the existence of faint sounds during the long silences between successive ventricular beats. I could not satisfy myself that I heard more than one such sound in each silence: it seemed to me to follow the second sound of the heart at varying intervals in successive beats. I noted also that the first sound of the heart varied markedly, for it was sometimes almost entirely replaced by the systolic bruit and at other times it was singularly thumping in character and quite unaccompanied by any bruit. During the time I devoted to watching this peculiarity it appeared to me that the thumping first sound occurred about every 8 or 9 beats but I cannot say that this was constant. I shall refer to this again later on.

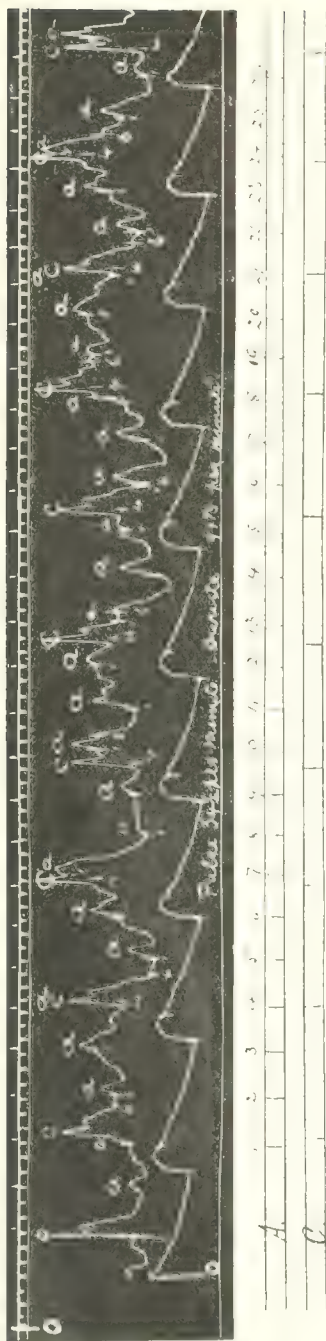


FIG. 3. Feb. 25th, 1911 (A : F : 17 : 6)

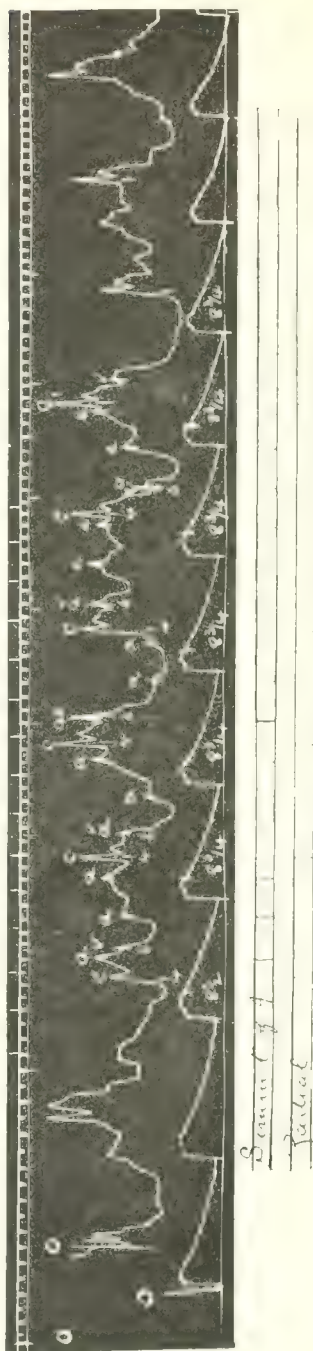
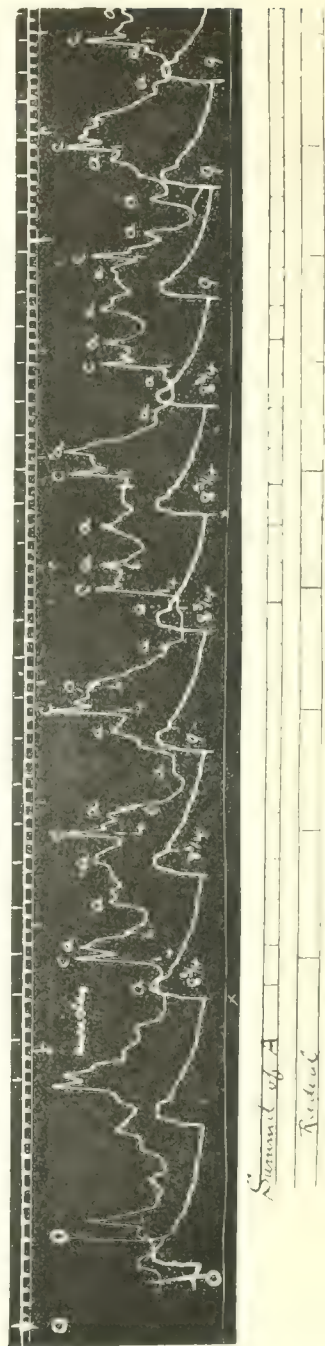


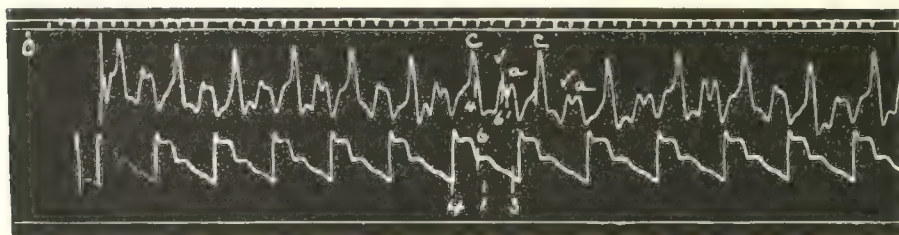
FIG. 4. Feb. 25th, 1911. Auricles 101, Ventricles 34 per minute.



CASE 2. Charles B., aged 51, was admitted under my care on July the 19th, 1910, complaining of 'rheumatism.' He stated that he had had rheumatic fever 35 years before. The history he gave us of an attack of gonorrhœa some 25 years ago, shortly before a return of the articular pains, the fact that the temporo-maxillary joints had been affected, that there was pain and swelling in the metacarpo-phalangeal articulations and that he had had several attacks of iritis made it clear that his rheumatism was at all events in part of gonorrhœal origin. He had been in the Infirmary some 20 years previously, when a diagnosis of ordinary rheumatism was apparently made. A special note appears in the record of the case that there was no affection of the heart, though occasional blueness of the lips was observed, and an inspection of the temperature chart on which the pulse rate is recorded shows that on no occasion did it fall below 70 and that it was usually above 80.

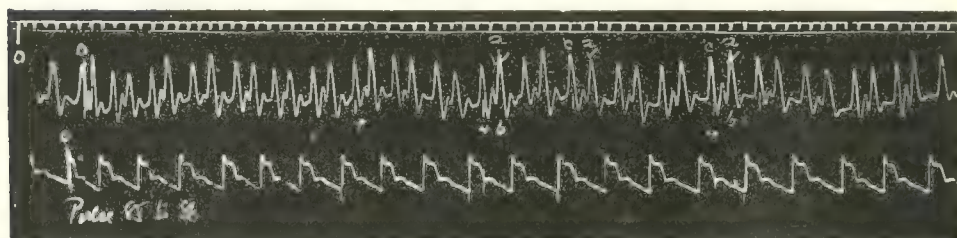
On his admission under my care, though he did not complain of any cardiac symptoms, a very ready diagnosis was made of aortic disease. The opinion was formed that there was a moderate amount of regurgitation with a certain degree of true stenosis. I was doubtful whether a faint systolic bruit at the apex was of mitral origin, and in that case due to secondary left ventricular dilatation, or whether it was merely the systolic aortic bruit transmitted. The patient remained under my care until he was discharged on December the 7th greatly improved; since then I have seen him frequently. He was treated with iodide of potash, of which he took 30 grains daily, from the date of his admission till August the 17th when it gave place to the syrup of the iodide of iron. The potash was resumed on October the 15th, when the patient began to take 45 grains daily, this dose being increased to 60 grains daily on the 23rd of the same month, a dose continued till his discharge. He was also treated with gonococcus vaccine and to this I shall return later.

He never had any considerable cardiac discomfort or dyspnœa and certainly nothing suggestive of the Stokes-Adams' syndrome. From the date of his admission till September the 8th his pulse usually varied from 60 to 86, being never more than this and falling below 60 on three occasions only, the records being 54, 58 and 54. On September the 8th the pulse dropped from 72 to 48, this change not being accompanied by any subjective phenomena. From then till October the 10th it remained below 50 except on four occasions, on one of which it reached 52 and on three of which it was counted at 50. On one occasion it went down to 42 and very often to 46 and 44. On October the 10th it reached the lowest rate recorded on the ward chart during this phase, and was counted at 40. The same evening it was 66, and from then till November the 11th it fell below 60 on two occasions only, being 56 on October the 13th and 52 on the 21st of that month. During this phase the pulse was more frequently above 70 than below that figure; it was often above 80 and on several occasions was above 100.



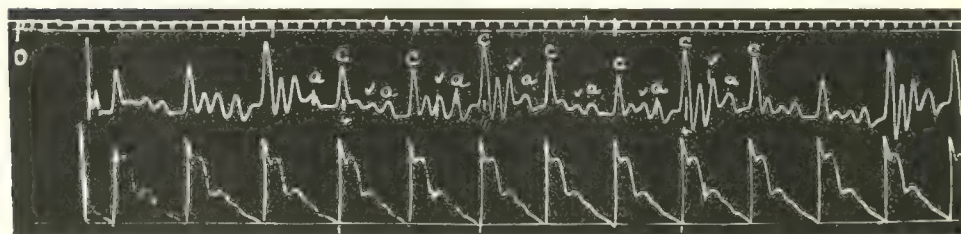
Arterio
ac just over 2 fifths
Cervical and ventricle

FIG. 6. Oct. 10th, 1910. Pulse 65.



Arterio
ac just over 2 fifths?
Cervical and ventricle

FIG. 7. Oct. 31st, 1910. Pulse 85-86.



ac = 2 fifths

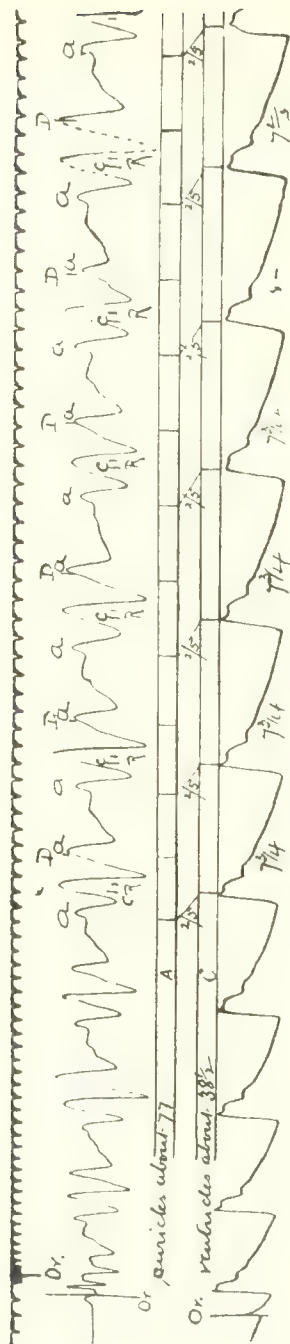
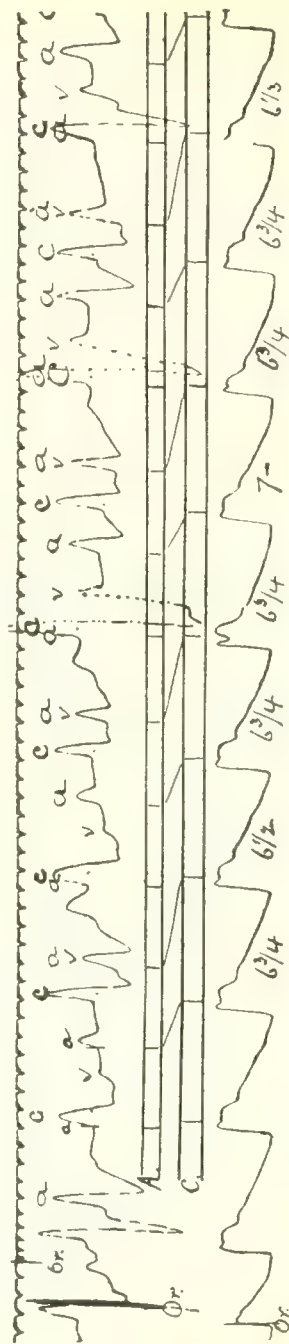
FIG. 8. May 24th, 1911. Pulse 62-63.

He had the first dose of gonococcus vaccine (5,000,000 organisms) on September the 7th, the day before his entry into the first slow phase of cardiac action. Subsequent and much larger doses, given during the phases both of frequent and of infrequent cardiac action, failed to show any effect on the pulse.

In this case very numerous tracings were made and I purpose discussing some of these, not in chronological order but in that which will best serve to illustrate the special points I desire to emphasise.

The tracings shown in Fig. 6, 7 and 8 were taken during the phases of frequent cardiac action, as may be seen from the dates. The explanatory key under each tracing has been modified from the usual form, the black oblong in the carotid and ventricular column being intended to show the total duration of the ventricular contraction. The small portion left unshaded will serve to indicate more clearly the actual length of the *a-c* interval which is of course slightly longer than the *As-Vs* interval. In Fig. 6 the *a-c* interval is seen to be just over two-fifths of a second. With this lengthened *a-c* interval and with the heart beating at 65 the auricle enters into contraction very shortly after the relaxation of the ventricle, an event which I have taken as occurring at the moment the ventricular wave in the venous pulse begins to fall. In the key to Fig. 6 this is indicated by the vertical line from the auricular systole falling clear of the black oblong which indicates the previous ventricular contraction. In Fig. 7 the heart is seen to be beating at the rate of 85 to 86; each ventricular wave becomes pregnant with the auricular wave of the following cardiac cycle, for the auricle enters into contraction before the ventricle has relaxed. This is indicated in the key by the vertical line from the auricular systole falling within the black oblong which indicates the previous ventricular contraction. In Fig. 8, which shows a pulse rate of 62 to 63 and in which the *a-c* interval is not more than two-fifths of a second in length, it will be seen that the auricular contraction falls quite clear of the previous ventricular contraction and that the *a* and *v* waves are quite separate. It would be difficult to interpret the tracing shown in Fig. 7 correctly, without the assistance of the other two, though its true nature might be suspected from the very pronounced and sharp *v* wave; but if the three tracings are studied together there can, I think, be but one conclusion. The precise length of the *a-c* interval in Fig. 7 cannot be determined with certainty, for the beginning of the auricular wave is obscured by the presence of the ventricular wave, *v*, with which it is coincident, and it may be shorter than I have represented it in the key.

In Fig. 9 the auricles are seen to be beating at 77 and the ventricles at exactly half that rate; every second auricular contraction is followed by a contraction of the ventricle at such a time that the *a-c* interval is two-fifths of a second. The time of the carotid impact is taken as one-tenth of a second prior to the radial, its actual incidence being obscured by the existence of a well marked post-auricular wave. The most obvious

FIG. 9. Sept. 8th, 1910. $a c = \frac{1}{2}$ FIG. 10. Sept. 9th, 1910. Auricles 66 6; ventricles 44.4 per minute; $a c = \frac{21''}{5}$ to $\frac{5''}{5}$ or $\frac{41''}{5}$

interpretation of this tracing is that every second auricular stimulus was blocked and that a condition of partial block prevailed.

In Fig. 10 the auricles are seen to be beating at 66.6 and the ventricles at 44.4 or two-thirds of that rate. An examination of the tracing would probably lead most observers, as it led me, to the view that every third auricular stimulus was blocked. Against this interpretation is the almost perfect uniformity in length of the successive pulse periods and, if it is adopted, we must assume that the passage of the second auricular stimulus is so sluggish that it leads to a ventricular contraction which occurs precisely midway between those which result from the more rapidly passing stimuli. As a rule I believe the blocking of every third stimulus leads to alternately short and long pulse periods but of course this is not an essential feature.

To assume that either of the two previous tracings was taken during a period of complete block and that the numerical relationship between the auricular and ventricular contractions was of the nature of a coincidence would be to adopt a view which no one would consider if the tracings stood by themselves.

Within a few minutes of the time the tracing shown in Fig. 10 was taken, with the patient lying in the same position and not being conscious of any change in his feelings, the tracing shown in Fig. 11 was secured. Now if we adopt the same view here, namely that every third auricular impulse is blocked, we shall find that there is a progressive lengthening of the *a-c* intervals, beginning from the ninth auricular systole, and if this view is persisted in we soon get to an impossible position. This is shown in the first of the keys printed below the tracing. An alternative view is indicated in the second key where the tenth auricular stimulus is assumed to be blocked; if after this we assume a block of every third auricular stimulus, we again find a progressive lengthening of the *a-c* intervals, and if we again attempt to evade the consequences of this by assuming that the fifteenth auricular stimulus is blocked, as is indicated in the third key, we again find the same progressive lengthening of the *a-c* intervals. Taking this tracing by itself, the conception of a complete block is the most natural one, though it must be noted that a pulse rate of 44 is higher than is usually noted in such cases. It is not likely that, in these two tracings (Fig. 10 and 11), we have records respectively of partial and of complete block, taken as they were within a few minutes of one another and characterised by the same pulse frequency. They are both probably examples of the same thing, that is to say either of complete or of partial heart-block. To the latter view I incline, though the difficulties, which its application to the interpretation of Fig. 11 involves are great. It may be that when two out of three impulses pass from the auricle to the ventricle this involves an amount of work which leads to exhaustion of the auriculo-ventricular bundle, manifested by a progressive lengthening of the *a-c* intervals and culminating in the second of these being ultimately blocked as is indicated by the asterisk in the second key to the figure. This leads to some recovery in conductivity and again two successive impulses succeed in passing, namely numbers 11 and 12; the blocking of number 13 improves the conductivity only so far that the *a-c* interval is

reduced to $3\frac{1}{5}$ -fifths of a second and again the next auricular stimulus, No. 15, is blocked, as is indicated by the asterisk in the third key diagram ; or it may be that the continuation of the second key represents the state of affairs, namely that 15 gets through and that the block affects 16 and 18.

The next two tracings, Fig. 12 and 13, show the presence of one extrasystole in each, and a study of these tracings is interesting though surrounded with difficulties. In the intercalated diagram of Fig. 12 I have simply shown the time relationships of the auricular systoles and carotid impacts ; in the subjoined key diagram I have attempted an interpretation. It starts on the conception of every third stimulus being blocked, and here again we find a gradual lengthening of the coupled *a-c* intervals as before. There can be no doubt that the beat which is marked by the asterisk is really an extrasystole ; it cannot be due to a normal stimulus coming from the auricle, for in that case the ninth auricular stimulus would have to be more rapid than the eighth. Regarding it as ventricular in origin, we may assume that the ninth auricular stimulus is blocked, this being in harmony with the third and sixth being blocked. If the ninth stimulus is blocked we may assume that the tenth passes through, as is suggested by the dotted line. There is of course no evidence in the presence of a ventricular systole that this stimulus really does pass, but it is in numerical series with numbers 1, 4 and 7, and if it reaches the ventricle during its refractory period there will of course be no direct evidence of its passage. Now if stimulus number 10 passes there should be a considerable delay in the passage of the next stimulus, which is not the case. I suppose it is possible to regard the extrasystole as being of auriculo-ventricular origin and arising in or about the node ; the slight sinus irregularity which prevails makes it impossible to say definitely whether the tenth auricular systole is or is not premature, so we cannot get assistance from that ; but if the extrasystole be really auriculo-ventricular in character then the conducting fibres will have had a longer rest and the undue shortening of the following *a-c* interval need not surprise us so much. On the basis of the block being a complete one and no stimuli passing from auricle to ventricle I suppose we would see in the practical identity in length of the post-extrasystolic pause and the usual pulse intervals an example of the peculiar rhythm described by Wenckebach in cases of complete block.

The next tracing, Fig. 13, on superficial inspection appears much the same, but in the first place the post-extrasystolic pause is distinctly longer than the usual pulse intervals of the rest of the tracing, and, in the second place, if we proceed on the basis of every third stimulus being blocked, we shall find we have to deal with an *a-c* interval which is progressively shortening and not lengthening as in tracing 12. Again the extrasystole occurs just after the more rapid passage of an auricular stimulus, which is not the case in Fig. 12. Let us regard the extrasystole as being ventricular in origin. It is not clear what happens to the 14th auricular stimulus. If there had not been any extrasystole it would doubtless have passed, being in series with numbers 2, 5, 8 and 11, and following on the short *a-c* interval of the 13th auricular stimulus. Probably however the occurrence of the extrasystole

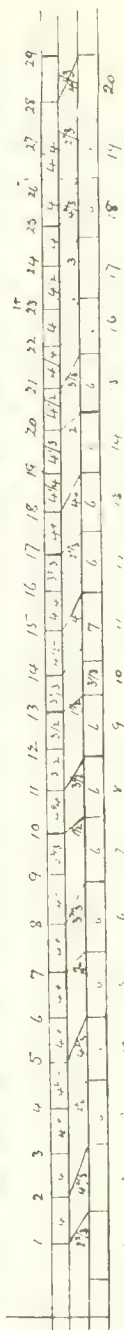
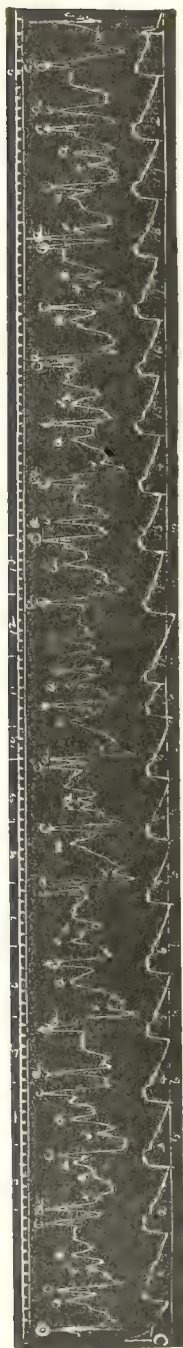


FIG 13. Sept. 28th, 1910.

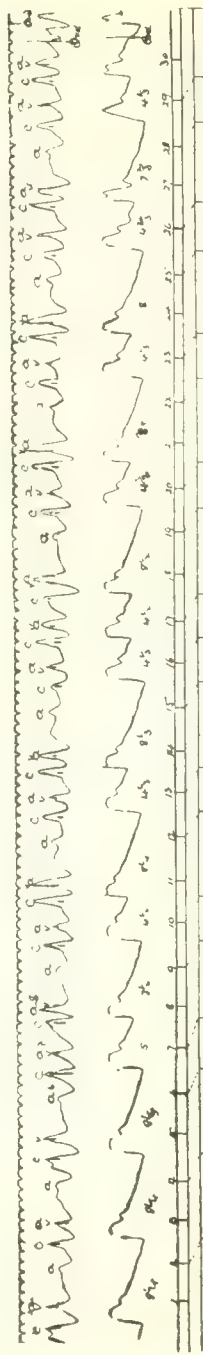


FIG. 14. Oct. 13th, 1910. In the key, the vertical lines represent the summits of auricular waves and the beginnings of radial upstrokes.

has led to the blocking of the 14th auricular stimulus, and, in consequence of this arrest in the work of the auriculo-ventricular bundle, the conducting media have had a longer rest, with the result that the 15th auricular stimulus passes through, though we should otherwise have expected it to be blocked, as it is in numerical series with the blocked stimuli numbered 3, 6, 9 and 12. In the latter part of the tracing we must assume that three auricular stimuli, namely numbers 20, 21 and 22, pass in succession for if number 22 is assumed to be blocked, then the next stimulus, that namely from number 23, must pass in one-fifth of a second; and if thereafter we adhere to the view that two beats of the auricle are effective in causing ventricular contractions and that the third is blocked, then the 26th auricular stimulus must pass in less than one-fifth of a second and when we come to the 29th we find that the *a-c* interval has lessened to extinction. Assuming the view expressed in the key, namely that 20, 21 and 22 all pass, the resumption of the condition in which the block affects every third stimulus again shows a progressive shortening of the *a-c* intervals as far as the tracing carries us. There is of course the possibility that the extrasystole is of auriculo-ventricular origin the stimulus reaching the auricle sooner than it reaches the ventricle.

The matter is not cleared up by a consideration of Fig. 14 and 15. In the former, if the view of a partial block is entertained, a difficulty is at once raised by the absence of any shortening of the *a-c* interval after the blocking of a stimulus or of any lengthening, except in the case of the 7th, when two or more pass in succession. This might make one incline to the view of the block being complete and to the short pulse spaces being due to extrasystoles of the kind described in complete heart-block by Wenckebach, which have already been referred to. The earlier pulse periods in the tracing are $8\frac{1}{4}$ fifths of a second in duration, indicating a pulse rate of between 36 and 37. Making allowance for the slight difference in frequency of the pulse, this part of the tracing was exactly like that shown in Fig. 9, the number of auricular beats being exactly double that of the ventricular and the *a-c* intervals, in association with every second auricular contraction, uniform in duration; this is a coincidence which is not likely to arise in heart-block if complete.

In Fig. 15 the same difficulties arise. On the view of a partial block we have the difficulty of the singular uniformity in the duration of the *a-c* interval under conditions of varying stress on the conducting structures; on the view of the block being complete we have to accept the latter part of the tracing as the expression of a continuous discharge of premature systoles of the ventricle of the kind described by Wenckebach and yet arising so uniformly that the *a-c* intervals are practically equal, a condition against which the odds are altogether overwhelming. The tracings taken on the same day showed long periods in which the same characters prevailed as are seen towards the end of the figure, namely a pulse rate of about 67 to 70 conforming in frequency with the auricular systoles and with a singularly uniform *a-c* interval, a condition which heightens the improbability of the block being a complete one.

In this second case therefore, the difficulty of determining whether the block is a complete or partial one, or whether it is sometimes the one and

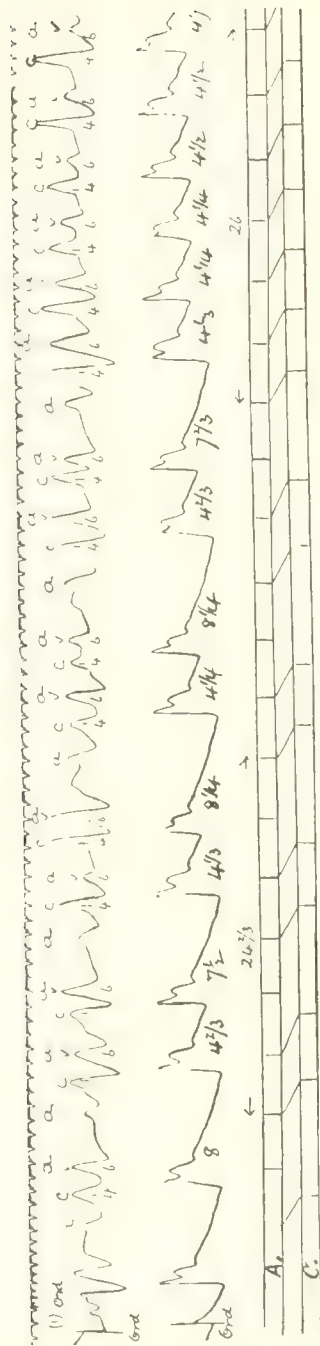


FIG. 15. Oct. 13th, 1910.

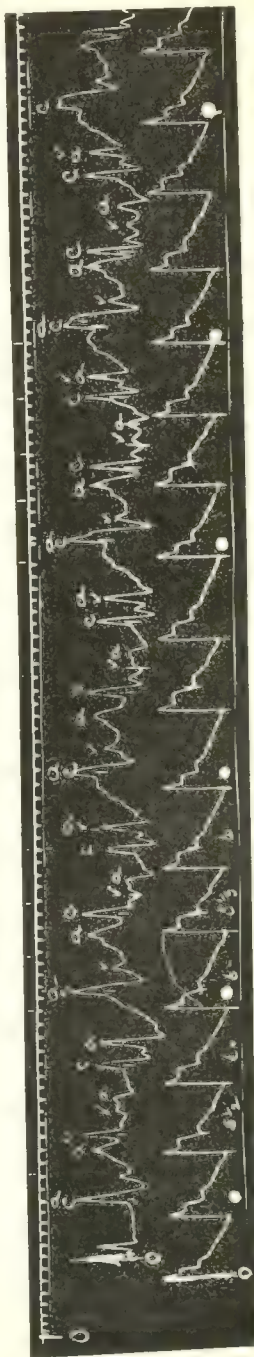


FIG. 16. Dec. 7th, 1910 Pulse rate 52.

sometimes the other, is very great. In discussing Fig. 11, 12 and 13, I have referred to the progressive lengthening of the *a-c* interval, which occurs in the two former, and to the shortening which occurs in the latter, and I have made some attempt to explain these changes on the basis of the block being a partial one. They are of course also explicable on the basis of the block being complete. If, as in Fig. 11 and 12, three interauricular spaces are less than two interventricular or pulse spaces, then, be the block partial or complete, there will be a progressive lengthening of the *a-c* interval; on the other hand if, as in Fig. 13, three interauricular spaces are more than two interventricular spaces, there will be a progressive shortening. If we revert for a moment to Fig. 9 and 10, we find that in the former two auricular spaces are exactly equal to one pulse period and that in the latter three auricular periods are exactly equal to two pulse periods: in consequence the former shows *a-c* intervals of uniform length and the latter alternately short and long *a-c* intervals, all the short ones being of the same length and all the long ones being of the same length. I commented on the improbability which might be supposed to attach to a perfect correspondence in length between say three auricular spaces and two ventricular spaces, but after all they must either be equal as they are in Fig. 10, or one group of events must exceed the other in duration, of which examples have just been given in Fig. 11, 12 and 13. It is the long continuance of a definite relationship, be it one of strict equality or of slight but constant excess on the part of one group or the other, that is so much against the existence of a complete block. Anything which tells against a partial block is in favour of the block being complete and I may here again point out that, in Fig. 10, 11, 12 and 13 on the one hand, and in Fig. 14 and 15 on the other, the same explanation, namely that of every third stimulus being blocked, involves us in the difficulty that in the former group there is a marked lengthening of the second period of conduction while in the latter the conduction periods are all practically equal. If we assume that the block is really a complete one, in spite, be it noted, of the fact that the ventricular rate is usually too high for the ready acceptance of this view, the interpretation of Fig. 12 becomes easier: for we note that the post-extrasystolic pause is equal to the ordinary pulse period, but the same does not hold good in Fig. 13, for here that period is distinctly longer, a point strongly against complete block. Of course a block may be at one time partial and at another complete, but in this case we are not helped by this consideration for we should have to assume very frequent changes and that these occurred without any subjective phenomena. Upon the whole, though some of the tracings point strongly to a condition of complete block, I incline to the opinion that the block has been a partial one throughout. This view seems to me to involve one in fewer and less formidable difficulties. I must admit that its acceptance may make it difficult logically to accept as certain my conclusion as to the completeness of the block in my first case. I shall not re-open that question for I think I have said enough to indicate some of the difficulties which arise in the distinction between partial and complete heart-block. If it be accepted that in the first case the block

was a complete one, the demonstration of a normal *a-c* interval very shortly before is noteworthy though this has been observed by others.

The auscultatory phenomenon to which I wish to call attention was noticed by me in *CASE 2* at a time when the pulse was beating infrequently. Subsequent observations showed that it occurred only when the auricular contractions were more frequent than the ventricular. The sign was a striking alteration in the character of the first sound of the heart as heard at the apex. Every few beats this was singularly thumping and emphatic in character, reminding one rather of the loud first sound which one gets in cases of mitral stenosis but duller than this. The abnormal sign sometimes appeared rhythmically every three or four beats, but at other times might not be heard for eight or nine beats, and on many occasions it was not to be heard at all. The sign was a very striking and obvious one and I confirmed my own impressions by getting my colleague, Dr. Barrs, and my house physician, Mr. A. E. Taylor, to listen independently. I then took the tracing shown in Fig. 16. Mr. Taylor auscultated the heart and every time he heard the first sound thudding in character he called out and I made a small mark on the passing tracing. These marks on the tracing have been enlarged into circles. The key printed below the tracing must not be taken as doing more than showing the number and time relationships of the auricular and ventricular systoles. I waive the question as to whether the block is a partial or a complete one. What the tracing does show is that when the thudding character of the first sound was observed the auricle and the ventricle began their contraction about the same time. Probably it is essential that the auricle should be in systole at the time when the ventricle enters into contraction for the production of this peculiar sign. When describing my first case I mentioned a similar occasional peculiarity of the first sound and pointed out that when this existed there was a disappearance of the systolic bruit at the apex. This patient did not come under my notice till I had made the above observations and I was not surprised on examining my tracings to find that from time to time the auricular and the ventricular systole coincided in time. In this case I was not able, being single-handed at the time I made the later tracings, to have simultaneous auscultatory observations made.

The last point on which I wish to comment is the appearance from time to time in *CASE 2* of the *pulsus alternans*. There are of course several conditions which lead to the appearance of alternately large and small beats at the wrist and we must clearly discriminate between the *pulsus bigeminus* and the *pulsus alternans*. If from any cause the ventricle contracts before its proper time the systole will be a feeble one and the arterial pulse will be small. This is of course no reflection on the cardiac musculature which has been called upon to contract before it has had time to store up energy. In the pulse the small beat is premature, the time between the large beat and the small one is less than that between the small beat and the large one, and we have here an example of the *pulsus bigeminus*. When however the ventricle enters into contraction at regular intervals and each alternate contraction is feeble, we find that the alternate

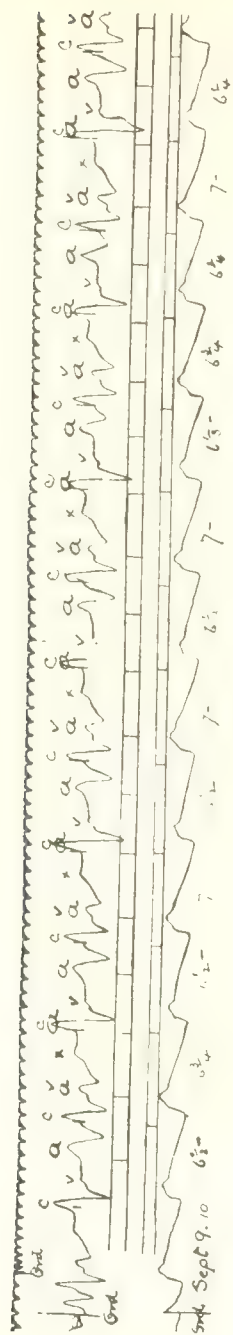


FIG. 17.

large and small arterial beats which result from this are more or less evenly spaced. The small beat is separated from the large one which precedes it by at least as great a period of time as separates it from the following more powerful beat : in other words the small beat is not a premature one, usually, indeed, it is slightly delayed, being the result of a feeble contraction of the ventricle. This is the *pulsus alternans* and it is usually regarded as carrying with it a very grave prognosis and as being a severe reflection on the cardiac musculature which has not the excuse afforded by a premature demand on its energies for a feeble response on every second occasion.

This condition of pulse is shown in Fig. 17. The smaller pulse beats are separated from the preceding beats by longer intervals than they are separated from those which succeed them. The venous tracing shows that the auriculo-ventricular ratio is as three to two. Again I waive the question as to the character of the block, whether it is complete or partial. Every third auricular systole corresponds in time with a contraction of the ventricle and it is always this effort of the ventricle which is attended with a small and delayed radial pulse. I think it must be somewhat of a handicap for the ventricle to contract at the same time as the auricle. There may be another explanation of this peculiarity in the pulse or more than one. I should think, but I cannot be sure, that the ventricle will find itself more fully charged with blood when it is about to enter on the contraction which leads to the larger radial pulse. If this is the case I can understand the alternately large and small pulse in the arteries, but I do not think this explanation will cover the delay in the smaller beat as manifested at the wrist. Be the explanation what it may, the point I desire to emphasise is that no gravity attaches to the appearance of the *pulsus alternans* under these circumstances and that there is no reflection on the ventricular musculature, which is sinned against rather than sinning. It was only when the auriculo-ventricular ratio was as three to two and when in addition there was a coincidence in time between every third auricular systole and every second ventricular systole that this *pulsus alternans* was observed, and it should be mentioned that these conditions did not always lead to its presence. The conditions prevail apparently in Fig. 10 and in the latter part of the tracing a very slight degree of true alternation may be seen, but in some of my tracings, though the conditions prevailed, there was not the slightest indication of its existence.

The influence of a dose of atropine in the accentuation of this condition should be mentioned. The tracing which shows the condition in an ill-marked form (Fig. 10) was taken just before the administration hypodermically of one-hundredth of a grain of atropine; that shown in Fig. 17 was taken very shortly after the drug had been given. The atropine did not produce any subjective phenomena nor did it increase the frequency of the auricular systoles, but a comparison of the two tracings and of others taken before and after the injection makes it clear that the condition was markedly accentuated by the drug. Whether the administration of atropine tends to cause an *alternans* action of the ventricle when the auriculo-ventricular rhythm is normal I am not able to say.

IRREGULARITY OF THE HEART'S ACTION IN HORSES AND ITS RELATIONSHIP TO FIBRILLATION OF THE AURICLES IN EXPERIMENT AND TO COMPLETE IRREGULARITY OF THE HUMAN HEART.

By THOMAS LEWIS.*

(*From the Cardiographic Department, University College Hospital Medical School*).

TOWARDS the termination of the observations made upon complete irregularity of the heart's action in the human subject, a full report of which was published in *Heart* in March, 1910, it occurred to me that if I could find a similar pathological affection in any of the lower animals, it might finally settle the nature of the irregularity with which I had to deal.

My clinical observations and my experiments all pointed in one direction, and I felt confident that the disorder of the ventricular movements was in reality the outcome of fibrillation of the auricles. The discovery of a similar irregularity in one of the lower mammalia would provide an opportunity of putting the matter to a direct test, for an animal so affected might be opened and the heart inspected as it beat *in situ*.

My attention was directed especially to the domesticated animals, for they have a similar environment to man and are under observation and control. I first thought of the dog, and made a number of enquiries in regard to the pathological mechanism of the heart in this animal, but eventually abandoned the search because of the marked respiratory arrhythmia which the dog exhibits. I had no hope of obtaining the material I required from this source, if it exists, for on account of its obvious rarity and the presence of the natural arrhythmia, I could neither collect it myself, nor rely upon the observations of others in identifying the irregularity sought.

Horses became the next subjects of search. The relative frequency with which these animals are vetted, and the regularity of the heart's action in horses suggested that they might be a suitable hunting ground; and I was encouraged by the description in several veterinary text books of a rare affection of the horse's heart under the term "tumultuous action of the heart." But I should not have been successful had it not been for the great kindness of Professor Woodruff of the Royal Veterinary College, and for that of Major-General F. Smith, who was then chief of the Royal Army Veterinary Corps. While Professor Woodruff arranged that a careful

* Working under the tenure of a Beit Memorial Research Fellowship.

search should be made amongst horses attending the out-patient department at the Veterinary College, General Smith very kindly sent circulars of enquiry to the various depôts under his command. I was able to interest a number of other veterinary men, both in London and the provinces. In this manner a very large number of animals came under observation from the required point of view; and, although the affection is of great rarity in horses, I have been fortunate enough to collect notes and observations upon five animals. These notes and observations are by no means complete. The difficulties connected with such work are considerable. It has to be carried out in places ill suited to it and observations are often hampered by the prejudice of the owner or by official restrictions. Nevertheless, the material which has been gathered seems of sufficient interest and importance to permit its publication in detail at the present time.

Horse 1. This animal was seen at Colchester through the courtesy of General Smith. It was a gelding cob of 15 hands $3\frac{1}{2}$ inches. The age was nine years. The horse had come under observation seven months previously, when it showed symptoms which prevented it from working. Irregularity of the heart's action was noted: when galloped a hundred yards the animal became acutely distressed, foaming at the mouth occurred, the breathing became laboured and eventually the animal staggered and fell. At times there was hæmorrhage from the nostrils. A large pulsation at the root of the neck and in the neck itself had been noted, and this was stated to be increased by exertion. There was rarely, if ever, any cyanosis. The arterial pulse was usually counted at 14-16 beats per minute.*

The animal was examined in its stable at Colchester on December the 4th, 1909. The pulse, which was palpable in the superficial temporal and submaxillary arteries, was feeble. Its rate lay between 20 and 50 per minute, varying very considerably from time to time. It was absolutely irregular in force and in rhythm. Sometimes a long pause was felt, sometimes a run of a few quick beats; at other times beats of very varying lengths followed each other irregularly. The pulse rate increased markedly (from 40 to 90 beats per minute) with light exercise. At the root of the neck pulsation of a general welling character was visible and it could be followed along the external jugular veins as far as the middle of the neck. It was easily palpable with the finger, and the veins in which it occurred were obviously distended. The pulsation was synchronous with the arterial pulsation, but slightly more frequent in its incidence. The heart was auscultated and the irregularity in its characteristic form could be clearly identified. The first and second heart sounds seemed clear, no adventitious sounds were audible. There was no cyanosis, but there was dropsy. The legs were puffy and the most dependent portions of the belly pitted very readily on pressure. A great deal of time was spent in attempts to obtain

* The normal rate is 35-40 beats per minute.

graphic records of the movements, but they were only partially successful. Simultaneous records were out of the question, on account of the restiveness of the animal. A few arterial and venous curves were obtained separately.

A short strip of arterial curve taken from the superficial temporal artery is shown in Fig. 1. The rate for the six beats shown is 43, and the beats have respective lengths, in fifths of seconds, of 10, 5, 6.3, 4.7, 6.4 and 9.0. Another strip in my possession shows beats in fifths of seconds as follows:—7.5, 11.8, 6.5, 9.2, 4.2, 11.2, 6.4, 7.4, 7.8, 6.0, 4.4, 15.7, 6.2, 7.8, 7.6, 13.3 6.3, 7.7, 13.7; an average rate of 32 beats per minute.

Strips of the venous pulsation in the external jugulars are shown in Fig. 2, 3 and 4. The pulsation was carefully timed subjectively, and the sharp upstroke ending in a pointed peak synchronised with the arterial pulsation. At times a beat was recorded from the veins when no pulsation in the artery was felt. The tracings of the venous pulsations are of the characteristic plateau form and during the diastole, where this is long, a stasis wave is seen and there are fine oscillations upon it, (especially well seen in the long pause of Fig. 3 and 4).

The animal was shot and a post-mortem was made. The pericardium was thickened and enveloped in fat. The mitral and tricuspid valves seemed a little thickened. The muscle of the ventricles was thick and friable. There were some large patches of fibrosis in the left auricle. The lungs, abdominal viscera and arteries appeared normal. The heart was sent to Dr. Cohn of New York.

Horse 2. The following notes are abstracted from a War Office report. The animal was 16 years of age and had seen 9 years service in the South Wales Borderers. It had been under observation for some while for poor condition and wasting: until 4 days before admission it had worked satisfactorily. It was brought to the sick lines on December the 28th, 1909, having refused its food. The pulse was counted at between 80 and 90. The temperature was 105.2° Fahr.* The respiration was hurried, 25 to the minute,† and there was evidence of pain, the animal looking continually round to the side. The horse refused food and water. Regurgitation through the jugulars was extraordinarily conspicuous, and quite apparent from the other end of the loose box in which it was stalled. On palpation it resembled an arterial pulse, so vigorous and strong was the beat. Congestion of the visible mucous membranes was present, but only slightly, and this probably by reason of the anæmic condition of the animal. Pain was manifested on manipulation of the cardiac area. Auscultation of the heart revealed a confused, irregular and excessive action of the heart.

Treatment was expectant. Mustard was applied over the ribs of the cardiac region. On the 29th the high temperature was maintained and the

* The normal temperature of the horse is 100.4–100.9° Fahr.

† The normal respiratory rate is 8–10 per minute.

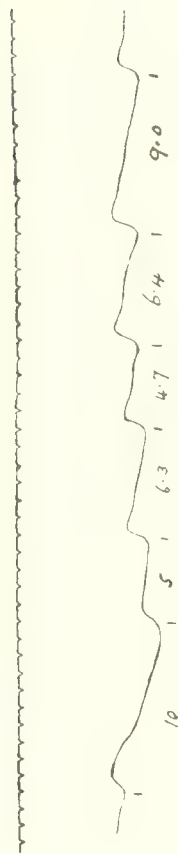


FIG. 1.

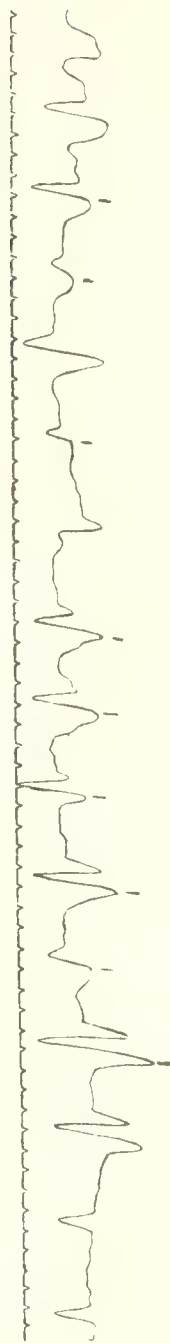


FIG. 2.

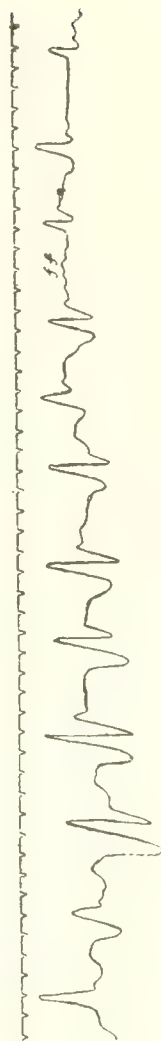


FIG. 3.



FIG. 4.

pulse was unaltered. The venous pulsation was less and the pain seemed relieved. A bran mash was eaten with some show of hunger. On the 30th the temperature fell to 102° and the pulse and respiration seemed improved: little or no jugular pulsation was evident. Hay and mashes were taken. The heart's action is said to have been normal on this day. On the 31st the temperature rose again, but no other symptoms reappeared. From this time until the night of January the 2nd the condition was unchanged. On that night a relapse occurred, the animal refused food and water and again showed evidence of pain. There is no note of the pulse condition at this time. On the morning of the 3rd, death occurred unexpectedly. The horse was found down in its stall with the neck bent under the body. He apparently fell suddenly and with great force against the iron manger, fracturing the cranium.

At the post-mortem the skull was found fractured. The heart appeared to be abnormal. It was unhealthy in colour, its walls were hypertrophied, a few white spots were visible on the endocardium, whilst the pericardium was also thickened and slightly dropsical. The valves were unaltered. The unexpected death of the horse precluded my seeing it.

Horse 3. The observations upon this mare were made through the kindness of Sir J. Macfadyean and Professor Woodruff.

It was a cart horse, aged 15 years, $16\frac{1}{2}$ hands in height. The past history was unknown. It was taken to the Veterinary College on account of breathlessness and staggering occasioned for some months by exertion.

I saw this horse on a number of occasions in January, 1910. The pulse was feeble and continuously and completely irregular: the rate was from 40-160 per minute. The heart sounds were clear; there were no murmurs. Little or no venous pulsation was visible in the neck while the animal stood in its stall, but it became prominent, and the rate of the heart beat increased, when it trotted a few hundred yards. The exertion also produced conspicuous dyspnoea.

Upon February the 12th, 1910, the horse was transported to some stables in the neighbourhood of University College Hospital Medical School and the stall was connected to the galvanometer. Curves were obtained by wrapping large pieces of cotton wool, soaked in saline, around metal electrodes and fastening these to the limbs or chest wall. The lead first adopted was from the right axilla to the left groin: curves were obtained which are exemplified in the third strip of Fig. 5. The curve may be compared with that taken from a horse by Einthoven (and published as Fig. 203 in Ellenberger and Schemert's "*Lehrbuch der vergleichenden Physiologie der Haussäugetiere*," Berlin, 1910). Take first the ventricular complexes marked *R*, *S* and *T*: these portions of the curves are almost precisely the same as the corresponding phases shown in Einthoven's curve of the normal horse. They are sufficient to show that the ventricular beats in the abnormal curve are all of supraventricular origin. In Einthoven's curve each

ventricular contraction is preceded by an auricular representative, *P*, which is as prominent as the *T* shown in this strip. All trace of such variation is absent in the present instance, clearly pointing to an absence of co-ordinate and presystolic contraction of the auricle. The beats of Fig. 5 (strip *III*) are irregularly spaced: they lie at distances of 2.7, 2.9, 3.7 and 4.7 fifths of a second apart. The irregularity is of the characteristic form exhibited by a fibrillating auricle. The first two strips have a larger excursion. They were taken by applying the right forelimb electrode to the epigastrium, the left hindlimb electrode to the breast beneath the root of the neck. Compared with the third strip they are consequently inverted. These curves show the same summits *R*, *S* and *T*, but again no signs of co-ordinate auricular contraction. The rate is very variable. The irregularity in spacing is extreme. The heights of the opening variations of systole (notably *S*) are not proportionate to the pauses which precede the corresponding beats. These features are one and all characteristic of experimental fibrillation and complete irregularity of the human heart. There remains but a single feature and that is the oscillation, which is so typical in many experimental and clinical instances and which is due to the fibrillating auricle. It is obscurely seen in several places in these curves (and is marked *f*, *f*).

The pauses from beat to beat in a succession of 8 strips are tabulated and are given in the accompanying table. The successive beats read in columns from above downwards.

PULSE BEATS IN ONE-FIFTH SECONDS IN 8 STRIPS.
AS CALCULATED FROM ELECTRIC CURVES.

3.1	4.1	3.3	2.6	2.2	4.0	3.5	3.0
3.3	3.4	3.4	4.8	2.0	2.4	3.3	3.0
3.2	4.6	4.0	2.8	1.8	4.9	2.5	3.2
3.3	2.7	2.7	2.9	1.7	3.4	3.0	3.7
2.3	4.8	2.8	2.7	1.7	3.1	3.6	2.6
3.8	3.1	3.7	4.0	2.1	3.8	3.4	2.5
3.4	3.2	4.6		2.0	2.7	2.7	3.7
2.1	3.0			2.7	4.5	2.9	4.9
2.0	2.4			2.2	3.1	3.1	3.5
3.2				1.8	2.5	3.0	4.0
3.4				1.7	2.3	3.9	5.6
4.8				1.9	2.2	2.6	4.3
5.3				1.7	3.6	3.0	4.6
2.7				2.1	4.1	3.5	3.6
				2.4	3.1	3.5	2.7
				2.3	2.5	4.7	4.6
				2.6	2.4	5.4	4.5
				2.0	3.1	4.7	3.1
				1.6	3.2	3.6	
				1.7	3.8	5.7	
				3.6	2.6	3.2	
				2.0	2.3	2.4	
				1.7	2.0	4.3	
					3.6	3.0	
					2.7	2.9	
					4.2	3.7	
					3.6	3.6	
						3.9	
						3.2	
						4.0	

On February the 19th the horse was killed by a shot in the head, the trachea was immediately opened and artificial respiration was established. The chest was opened through an incision in the right chest wall by sawing through a rib. Unhappily, during the removal of the rib, the ventricle was damaged and considerable hæmorrhage occurred. There was, nevertheless, sufficient time for certain observations. The ventricle beat rapidly and irregularly, while the auricle seemed to be standing still. On catching hold of the ventricle and moving it, so as to obtain a closer view of the auricle, the former passed into fibrillation. A closer inspection of the right auricle now revealed the presence of a fine fibrillary movement in its walls. The movement was watched for some minutes, in fact till no visible contractions could be made out in either ventricle or auricle.

As a result of these observations I am able to state that in a horse which presented the characteristic irregularity, the ventricular beat was co-ordinate and of supraventricular origin, and further that the co-ordinate contraction in the auricle was in abeyance. I am unable to state that while the ventricle was beating co-ordinately the auricle was seen to be in fibrillation. But it was not contracting co-ordinately while the ventricle was beating in this fashion and it was seen to be fibrillating within a few seconds of the onset of ventricular fibrillation. We know quite definitely that fibrillation is not transmitted from ventricle to auricle, and we therefore have strong presumptive evidence that the auricle was fibrillating throughout. That the mechanism of the heart was not altered by the cerebral death of the horse is clearly shown by the continued irregular ventricular action. There is but a single source of error; it is possible that the same application of the hand and movement which induced fibrillation in the ventricle also induced fibrillation in the auricle, which was previously paralysed. But such an occurrence is in the highest degree improbable.

The heart was preserved. Its weight was 5,440 grammes.* It was sent to Dr. Cohn of New York. There was some dropsy of the subcutaneous tissues; the arteries and other organs seemed normal.

Horse 4. An old gelding of about 15 hands, the exact age and history of which was uncertain, was brought to University College Medical School from the Veterinary College on February the 18th, 1910. It was examined in the street. The animal was in a distressed condition. Dyspnœa was marked, there was some dropsy of the legs and abdominal parietes. It presented violent pulsation of the whole neck, which reached as high as the ears. It was obviously venous, and, so far as could be ascertained, systolic in time. The pulsation and the heart's sounds were extremely rapid, averaging 150 beats per minute; the several beats followed each other in the most confused and irregular manner. There were no murmurs.

* The heart weight for medium-sized horses is given at 3 to 3.5 kilo, by veterinary text books.

Further observations were not possible ; and I was unable to purchase the animal or make any further investigation of it.

Horse 5. This horse was a gelding, aged 16, in height $15\frac{1}{2}$ hands. It was seen through the kindness of General Smith and Colonel L. Blenkinsop of Salisbury.

The symptoms had been present for 7 months. It had been under observation for 7 years, and was not known to have suffered from strangles or any other illness. The symptomatology consisted of very irregular and tumultuous action of the heart, marked breathlessness, epistaxis, faltering and occasionally falling, upon moderate exertion.

The horse was examined on Bulford Plain on June the 25th, 1910. The heart was absolutely irregular, long pauses of 2 seconds were frequent and short runs of rapid beats were noted from time to time. The rate was from 40 to 60 beats per minute, while resting. Upon exertion the rate showed increase, and a welling pulsation, not marked but distinct, appeared at the root of the neck. Breathlessness was fairly conspicuous after the animal had cantered a few times round a small paddock. The heart sounds were clear, there were no murmurs. The heart beats were more numerous than the arterial pulsations.

The horse was thrown in a covered yard and was chloroformed. It was then shot in the head, in compliance with the regulations, and the windpipe was opened. A good deal of blood poured from the trachea ; the shot had broken the base of the skull. As a consequence, artificial respiration was not free. The chest was opened by an incision on the right side and the removal of two ribs, and an excellent view of the beating heart was obtained. The ventricular movements were forcible and the spacing of the beats corresponded with what had been heard at the previous examination. For the horse they were rapid, and the irregularity was extreme. The ventricle showed no distension. At first no intrinsic movements could be seen in the auricle, it appeared to lie still except for the tugging transmitted from the ventricle. There was certainly no general shortening of its fibres. Closer inspection of the musculature revealed the presence of fibrillary movements. The epicardium covering the right auricle in the horse is comparatively thick and opaque and fibrillary movements are not readily seen in the underlying muscle. Close inspection of the ridges and, more especially, attention to the light reflections on its surface, particularly in the neighbourhood of the appendix, were conclusive. The independent movements of the several light reflections and the activity of the tissues generally was well displayed and was demonstrated to and recognised by the bystanders, including Colonel Blenkinsop. They were watched for several minutes, the ventricle continuing its active co-ordinate but irregular movements during the whole of this time. A hand was then placed under the ventricle, which was commencing to dilate, and in lifting it out of the pericardium it fibrillated. The auricle continued to fibrillate as before ; the two chambers were watched until all movements ceased in them.

The heart was removed, preserved and sent with the other specimens to Dr. Cohn. It weighed 4.335 grammes. The muscle was dark and friable. The pericardium and arteries seemed normal. The other organs presented little or no change.

Horse 6. While at Bulford Camp, I was shown another horse, stalled in the sick lines, by Colonel Blenkinsop. It was an old horse, suffering from chronic arthritic trouble. The heart beat at a normal rate, at or about 37 per minute. The beats followed each other perfectly regularly for about 10 or 15 cycles; a premature beat was then audible and it was followed after a prolonged pause by a further sequence of quite regular beats at the previous rate.

The irregularity obviously belongs to a distinct category: it corresponds to the single interruptions of a regular rhythm by pathological impulses in the human subject.

DISCUSSION.

The foregoing observations are sufficient to establish several facts. The horse suffers on rare occasions from irregularity of the heart's action, and the irregularity may be due to the presence of isolated premature contractions (*Horse 6*), or to a high grade of disorder in which the irregularity is complete. The completeness of the last irregularity has been observed in four separate animals and in two of these (*Horses 1 and 5*) graphic records have been obtained, confirming the subjective findings. The heart rate is variable but is generally increased. In the normal horse the rate lies between 35 and 40 per minute. When the gross irregularity is present the rate of the pulse may be decreased, presumably as a result of dropped beats; the heart rate on the other hand may accelerate to rates of 160 per minute for brief or long periods. The electrocardiograms (*Horse 5*) show that the irregularly beating ventricle is governed by impulses which descend to it through the auriculo-ventricular bundle and its branches; in every other way they correspond to the curves obtained in complete heart irregularity as it is observed in the human subject, and to the curves of auricular fibrillation as observed in experiment.

In two animals, from one of which graphic records were obtained, an inspection of the heart, beating *in situ*, revealed, first an irregularly beating ventricle and secondly a pulsationless auricle. In both, fibrillation of the auricle was witnessed. In the first of these observations (*Horse 5*) damage was done to the ventricle in opening the chest and there may be some doubt as to whether the auricular fibrillation did not follow upon this damage. This doubt is removed, for a precisely similar phenomenon was seen in the second observation (*Horse 5*), and in this instance no such damage occurred. The heart, at the inspection of it, was beating actively and was in good condition.

The presence of the same form of mechanism before and after the cerebral death of the animals and the resection of the ribs can scarcely be doubted, for the ventricular action remained constant throughout the whole of the preliminary procedures in both instances.

We are left with the conclusion that chronic fibrillation of the auricle is a pathological fact in horses, and that it is associated with an action of the heart which is in every way similar to that known as complete irregularity of the heart in man and to the irregularity which supervenes when the auricles are forced into fibrillation in the dog or cat.

Taking this evidence and that which has been previously recorded into consideration, the final conclusion that the three ventricular irregularities, namely, that which is found in the horse, that which is observed in man and that which is induced in the dog or cat, are one and the same seems indisputable. They are all dependent upon one underlying factor, namely inordinate or fibrillary contraction of the auricular tissues.

It is of interest to observe that in none of the five instances of auricular fibrillation in the horse was there any definite evidence of valvular lesion. It is known that in many of the human patients the valve segments are intact. The underlying mischief must be sought in the musculature itself. It is with this in mind and with a view to the eventual comparison of the human and equine material that I have asked my friend Dr. Cohn, whose knowledge of these muscle changes is so full, to undertake a detailed examination of the hearts which I have been able to obtain.*

CONCLUSIONS.

1. Horses are on rare occasions the subjects of two forms of irregularity of the heart. One of these consists of isolated premature contractions. The other is a complete irregularity.

2. The complete irregularity which occurs in the action of the ventricle of horses may be seen, from inspection of the heart as it beats *in situ*, to be associated with fibrillation of the auricles: a condition which must therefore be held as a proved pathological condition in these animals.

3. Fibrillation of the auricles in horses gives rise to a condition in which the symptomatology, and especially the graphic records, are identical in all their classical features, with a condition known as complete irregularity of the heart in man.

4. Complete irregularity of the heart in man is unquestionably associated with fibrillation of the auricles.

5. Fibrillation of the auricles in horses is usually unaccompanied by valvular lesions. It is accompanied by grave circulatory troubles which may be classed under the general term of heart failure.

* Brief reports of the continuing work have been published in *Heart*, 1909-10, i, 306, in the *Verhandl. d. deutsch. pathol. Ges.*, 1910, 112, and in the *Mechanism of the Heart beat*, London, 1911.

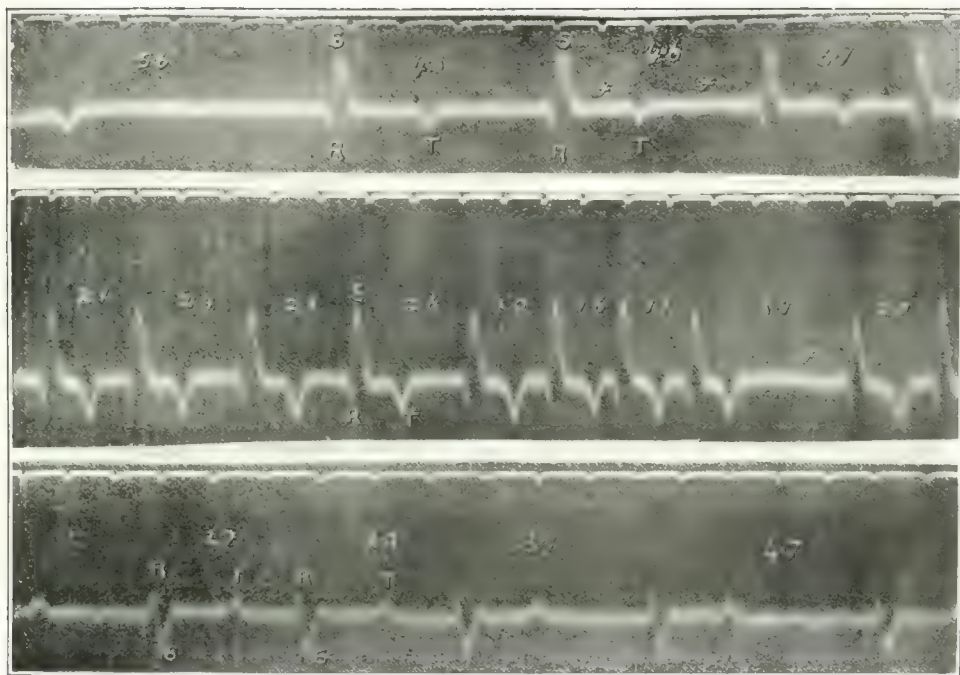


Fig. 5 (—). Three electrocardiograms from the third horse, the last strip is from the right fore-limb and left hind limb. Complete irregularity of the heart is present, each heart cycle is represented by *R*, a large *S* and a *T* variation, there is no sign of *P*. There are traces of oscillations in the longest diastolic periods shown.

The first two strips were taken from the epigastrium and centre of the breast in front; (they are consequently inverted). They show the same characters as those exhibited by the third strip. The irregularity is of high grade, the heart rate at times exceeds 150 per minute (normal 35-40). Oscillations are most distinct in the first strip. *P* is completely absent.

THE RELATION OF REGULAR TACHYCARDIAS OF AURICULAR ORIGIN TO AURICULAR FIBRILLATION.

BY THOMAS LEWIS* AND H. G. SCHLEITER.

(From the Cardiographic Department, University College Hospital Medical School).

IN the present communication we wish to record two cases of paroxysmal tachycardia which present features of exceptional interest. We utilize these two cases to illustrate the main thesis of this paper, namely, the close pathogenetic relation of regular tachycardia arising from an abnormal auricular focus and auricular fibrillation. The cases are of importance in that they support the general hypothesis that auricular fibrillation consists of an exaggeration of the phenomenon of pathological or heterogenetic impulse formation, which accounts for a large group of simple tachycardias arising in the auricle.

CASE 1. Paroxysms of auricular fibrillation. On one occasion a recorded paroxysm started as fibrillation and terminated as a regular tachycardia, springing from an ectopic auricular focus.

A. J., a cabinet maker of 28 years, was first seen on November the 11th, 1910, at the out-patient department at the City of London Hospital, in an attack of paroxysmal tachycardia. He has been under observation since that date and a number of paroxysms have been observed.

History.—His mother died of "heart disease" 14 years ago, she is said to have had rheumatic fever. A letter from Dr. Hargrave, who attended her in her last illness, tells us that she succumbed to progressive failure of the heart, which resulted from asthma and chronic bronchitis. His brothers and sisters, of whom four are alive, have never suffered from tonsillitis, rheumatism, chorea or heart disease. His two children are alive and healthy. One sister died of enteric.

Personally he has had no previous illness, excepting measles as a child and an occasional cold. Rheumatic affections and syphilis are denied. He has always been moderate in the consumption of alcohol and tobacco.

Two years ago he had his first heart attack, and since that time has been subject to them at intervals of 1-3 months. He attributes the first attack to strain, as it came on while he was lifting a heavy piece of furniture. The attacks usually last 15-18 hours. Lately they have been more frequent and some have lasted longer. The shortest attack has been 7 hours, the longest 3½ days. He states that the attacks come on at any time; they have often commenced in the night; exertion predisposes to them. They are not influenced by diet, so far as he knows. They commence quite abruptly and end in the same fashion; the cessation is always marked by considerable relief.

The first symptoms of the attack are faintness and sweating, a few minutes later he becomes conscious of palpitation, and feels cold and sick. Vomiting is said to occur ½-1 hour later, and about the same time he is aware of a fixed pain in the front and lower part of the chest. A

* Working under the tenure of a Beit Memorial Research Fellowship.

little later, the pain increases and is more prominent at the pit of the stomach and over the right ribs. It also radiates to the shoulders. He becomes very exhausted, thirsty and short of breath. Flatulence is a prominent symptom of the attacks and may precede them.

Between the attacks he is fairly well. He can walk in comfort, but easily gets giddy. If he is sitting and rises suddenly, the giddiness may cause unsteadiness and he supports himself, fearing a fall. He sometimes gets a little breathless after walking up one short flight of stairs. The appetite is good and he sleeps well; the bowels are opened regularly. He suffers from wind, and has had vomiting during the past few months. On several occasions, bright blood has been brought up.

During the last six months, he has done no work. He has lost ten pounds in weight in the past two years.

Observations between the attacks.—The patient is well built and nourished. He has a healthy, in fact somewhat excessive, colour. There is no trace of cyanosis. The lungs are normal; the nervous and alimentary systems present no objective signs of disease. The urine is normal.

The liver dulness extends from the upper border of the 6th rib to the costal margin, its edge is not palpable. The spleen is not felt. The thyroid and lymphatic glands are normal. The limits of cardiac dulness are normal, lying 0 and $3\frac{1}{2}$ inches to right and left of the mid-sternal line. At the apex there is a short systolic thrill and a harsh systolic murmur. Otherwise the heart sounds are normal. The arteries are somewhat thickened; the systolic blood pressure varies between 70 and 120 mm.Hg., (Riva Rocci). The heart beats regularly as a rule (Fig. 1 and 8). Its rate lies between 50 and 78 per minute. At times, sinus irregularity has been present. The *a-c* interval is usually one-fifth of a second in length (Fig. 1). During the stays in hospitals, his temperature has always been normal.

Observations during the attacks.—On three occasions, he has been admitted to the City of London Hospital in attacks (November the 9th, 1910, December the 8th, 1910, and August the 4th, 1911); he stayed at Mount Vernon Hospital from February the 2nd till March the 11th, 1911, and on two occasions he has been taken in at University College Hospital for attacks (May the 31st and July the 1st, 1911). During his last stay at University College he developed an additional attack. On no other occasion has a paroxysm commenced during his hospital stays, most of which have been of several weeks or months duration.

The attacks which have been observed have all been of over 12 hours duration and on one occasion a paroxysm lasted $3\frac{1}{2}$ days.

Seen within half an hour of the onset he is already distressed. The face is pale and sunken; he is restless and complains of distress of breathing and precordial pain. As the attack progresses his symptoms become aggravated, some cyanosis appears, the respirations increase in rate and the pallor becomes more conspicuous. The heart dilates and the liver becomes swollen and pulsates. Dropsy has not been noticed, and there have been no physical signs of œdema of the lungs. He is salivated during the attacks, develops a cough and when they have lasted many hours commences to expectorate a little frothy mucus.

The swelling of the heart may be exemplified by the following observations. When originally seen during a paroxysm in November, 1910, the measurements on percussion were $\frac{1}{2}$ and $5\frac{1}{2}$ inches respectively. At the end of a long paroxysm of 24 hours duration, on May the 31st, 1911, they were 2 and $5\frac{1}{2}$ inches. 5 hours after the cessation of the same paroxysm they were $\frac{3}{4}$ and $3\frac{1}{2}$. On July the 1st, they were 2 and $6\frac{1}{2}$ inches, 2 hours after the onset. 7 hours subsequent to the offset of the attack they were 0 and 4. 15 minutes after the onset of the attack of July the 15th, they were 0 and $5\frac{1}{2}$, the patient lying quietly in bed; a few minutes' restiveness was accompanied by a decided increase in the dull area. A definite and striking change to $\frac{3}{4}$ and $6\frac{1}{2}$ inches was observed and it persisted. 1 hour later, the paroxysm continuing, the measurements were recorded at $1\frac{1}{2}$ and $6\frac{1}{2}$. Next morning the paroxysm had ended and the limits were 0 and $4\frac{1}{4}$.

The nature of the paroxysms.—The majority of the paroxysms have consisted of attacks of auricular fibrillation, during which the heart rate has varied between 155 and 200 per minute. At such times the venous pulse has been of the ventricular form. Paroxysms of this nature have been observed and recorded on five occasions; examples of the curves are shown in Fig. 3, 4 and 10.

The second form of paroxysm, which was recorded electrocardiographically on one occasion only, consisted of a regular tachycardia, the average rate of which was 140 per minute. It arose from an ectopic focus in the auricle and formed the termination of a long paroxysm which commenced as fibrillation (Fig. 2 and 9).

The graphic records of observed attacks are summarised in the following table.

1st paroxysm.	9 XI 1910.	Auricular fibrillation (lasting many hours). (Venous curves).
2nd paroxysm.	8 XII 1910.	Regular paroxysm. (Lasting approximately 12 hours). (Venous curves taken but mislaid).
3rd paroxysm.	25/II/1911.	Auricular fibrillation. (Lasting 10 hours).
4th paroxysm.	31/V/1911.	Auricular fibrillation. (Lasting 12 hours). (Electrocardiograms, 3 leads).
5th paroxysm.	1/VII/1911.	Auricular fibrillation. (Lasting $3\frac{1}{2}$ days). (Electrocardiograms, 3 leads, Fig. 10.)
	2/VII/1911.	Tachycardia of auricular origin. (Electrocardiograms, 3 leads, Fig. 9 and venous curve, Fig. 2).
6th paroxysm.	15/VII/1911.	Auricular fibrillation. (Lasting about 10 hours). (Polygraphic curves and electrocardiograms, 3 leads).
7th paroxysm.	4/VIII/1911.	Auricular fibrillation. (Lasting approximately 24 hours). (Polygraphic curves)

Control curves of the normal rhythm were taken on a number of occasions, (1/VI/1911, 4/VII/1911, 14/VII/1911, 19/VII/1911, 21/VII/1911, 24/VII/1911, etc.).

The polygraphic curves are exemplified by Fig. 1-4. The curves are not treated chronologically. Fig. 1 shows venous and radial curves, taken on July the 21st, 1911, during a period when the pulse was slow (63 per minute) and regular. The *a-c* interval is one-fifth of a second.

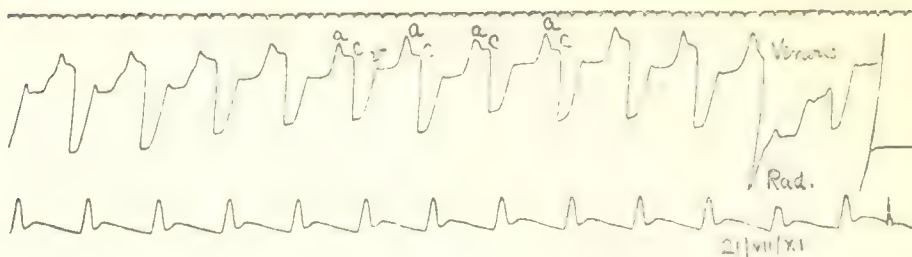


Fig. 1. *CASE 1.* A polygraphic curve taken while the heart's action was slow and regular. The *a-c* interval is $1\frac{1}{5}$ sec.. The pulse rate is 63 per minute. (July the 21st, 1911). The time marker of all the polygraphic curves is in $1\frac{1}{5}$ sec..

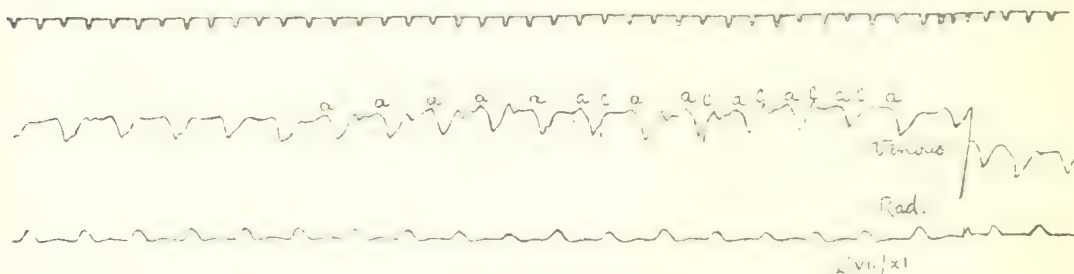


Fig. 2. *CASE 1.* A polygraphic curve taken during the long paroxysm observed on July the 2nd, 1911. The heart's action is regular; the rate is 142 per minute; the *a-c* interval is a full $1\frac{1}{5}$ sec..

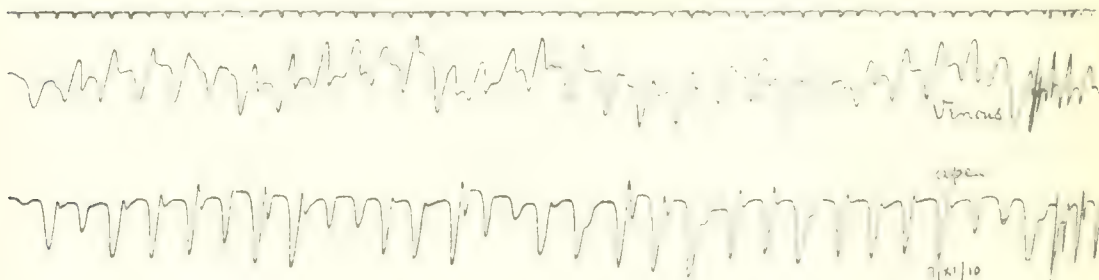


Fig. 3. *CASE 1.* A jugular and apex curve, taken during a paroxysm of tachycardia, (November the 9th, 1910). The heart's action is irregular; the rate is 165 per minute. The jugular pulse is of the ventricular form.

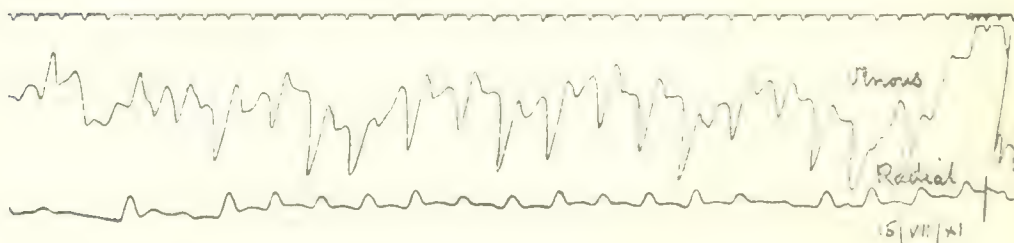


Fig. 4. *CASE 1.* A jugular and radial curve taken during a paroxysm of tachycardia, (July the 15th, 1911). The heart's action is irregular; the rate is 155 per minute. The jugular pulse is of the ventricular form.

Fig. 2 shows venous and radial curves taken at the end of a paroxysm on July the 2nd, 1911. The heart's action is regular; its rate is 142 per minute. The *a* wave is small and obscure. The *a-c* interval is one-fifth of a second. A number of observations were made upon the effect of certain events upon the rate of this paroxysm. Repeated swallowing had no influence on the rate. Changing from the sitting to the lying posture did not influence the heart's rate by more than two beats per minute. Repeated suspension of respiration had little or no influence upon the rate.

Fig. 3 and 4 are examples of curves taken during paroxysms on November the 9th, 1910 and July the 15th, 1911, respectively. Fig. 3 shows a venous and apical curve, Fig. 4 shows a venous and radial curve; in both, the heart is beating irregularly and the venous curve is of the ventricular form.

Electrocardiograms of the three separate mechanisms are shown in Fig. 8, 9 and 10. Each figure includes a series of three leads, marked *I*, *II* and *III* respectively. These represent Einthoven's usual leads in each instance: *I*, right arm to left arm; *II*, right arm to left leg; *III*, left arm to left leg. In each series the second lead is standardized so that 1/1,000 volt equals 0.6 cm. in the reduced curve.

The curves are not treated in chronological order. They are simply given as examples of the mechanisms which have been observed.

The normal mechanism has been recorded electrocardiographically on two occasions, on June the 1st, 1911 and on July 4th, 1911. The curves are identical for the two dates. Speaking of Fig. 8, each cardiac cycle of the regular mechanism shows auricular (*P*) and ventricular (*R*, *S* and *T*) representatives. *P* is prominent and bifurcates at its summit in leads *I* and *III*. The *P-R* interval is 0.14 sec.. The rate of the heart beat is 65 per minute.

This series should be compared with the two following series, Fig. 9 and 10. Fig. 9 was taken during the regular paroxysm of July the 2nd, 1911. Lead *I* shows *R* and *T* summits. *T* is inverted. (The first lead of the normal mechanism, Fig. 8, shows no *T* summit). *P* is very indistinct in this lead. In the second lead *R* and *T* waves are well represented; *R* is of less amplitude than in the normal mechanism. In Fig. 9 *II*, *P* is clearly represented as a complex curve, consisting of downward, upward and downward deviations. The third lead shows a diminished *R*, an increased *S* and an upright *T*. *P* is very similar to that found in lead *II*. The rate of heart-beat in this figure is 140 per minute. The *P-R* interval is approximately 0.18 sec. in duration. Comparing the two series of curves, it is seen that the ventricular complexes of the tachycardia and normal rhythm, Fig. 8 and 9, correspond fairly closely in the respective leads: the variations are chiefly in the amplitude of the various summits, and in an occasional inversion of *T*. The resemblance is sufficiently close to allow us to conclude that the origin of the heart beat is supraventricular during the tachycardia. The auricular origin of the paroxysm is proved by the presence of the clear auricular representatives in leads *II* and *III*. Nevertheless, the paroxysm

has originated in a focus at some distance from the natural pace-maker, as is indicated by the anomalous appearance of these auricular representatives. At the time when the electrocardiograms of the regular paroxysms were obtained, the movements of the string were watched and occasional premature contractions, interrupting the paroxysm itself, were observed, but were not recorded. The ventricular portion of such cycles seemed to give exactly similar electric complexes to those of the remaining paroxysmal cycles. The premature contractions, therefore, were presumably of auricular origin also.

The third mechanism is shown in Fig. 10, curves taken on July the 1st, 1911. They are from the beginning of the paroxysm of which Fig. 9 shows the termination. Similar curves were obtained on May the 31st, 1911, and on July the 15th, 1911. The ventricular complexes in Fig. 10 are similar in the three leads to those of the corresponding leads in Fig. 9. The beats are placed at quite irregular intervals throughout the curves. The rate is variable, but at times it reaches nearly 200 per minute. *P* summits are entirely absent in all the curves. No two adjacent cycles are exactly alike. The slight variation from cycle to cycle is due to the presence of the characteristic oscillations of auricular fibrillation, which are most conspicuous where the diastoles are relatively long, (*f.f.*)

CASE 2. Short and long paroxysms of tachycardia; the majority of the paroxysms were short and consisted of regular tachycardias springing from an abnormal focus in the auricle. They were occasionally interrupted by beats from a second abnormal auricular focus. On one occasion, curves showing the passage from the regular mechanism to auricular fibrillation were obtained.

G. T., a married man, aged 71, came to the City of London Hospital on May the 28th, 1911, complaining of chronic cough, pain in the chest and lower part of the back, together with occasional stiffness in the right upper limb.

History. The father and mother died at the ages of 81 and 77 respectively. Five brothers are dead, one, it is said, of heart disease; one sister is alive and in good health. He has had twelve children, four of whom died in infancy; of the remaining eight, one is tuberculous and the others are healthy. The wife, aged 52, has had one miscarriage. The patient, formerly a wood carver, is now an old age pensioner. In infancy he had measles and whooping cough. At the age of 51, he was in the Bethnal Green Infirmary for pleurisy and inflammation of the lungs. A few years later he had rheumatic fever. He states that he was laid up three years ago with a second attack of pneumonia. On the whole he affirms that he has enjoyed fair health. He denies venereal infection. In his younger days he drank ale freely. As a smoker, he has been moderate.

His present illness dates from 1908, when he first experienced cough and pain in the chest and lower part of the back. For the most part, pain has been referred to the precordium. It is gnawing in character and is related to meals. Sometimes it is said to have been so severe as to make breathing difficult, a feature which suggests for it a cardiac origin. Shortness of breath and palpitation of the heart have been noticed upon exertion. He has suffered from, and still has, a chronic cough with a slight expectoration of mucus. There has been no hæmoptysis. His appetite is poor, he sleeps badly and gets up at night to pass water.

Observations between the attacks of tachycardia.—The patient is an undersized and poorly nourished individual. His skin is sallow. There is no œdema or cyanosis. The veins of the lower limbs are varicose. There is extensive pyorrhœa. The thyroid is not enlarged. There is evidence of a mild degree of emphysema. There are fine crepitations at both bases. The nervous and alimentary systems present no signs of importance.

The heart's apex beat is in the 5th interspace, $4\frac{3}{4}$ inches to the left of the middle line. There is systolic retraction in the 5th interspace internal to the apex. The limits of the heart's dullness lie 0 and $4\frac{3}{4}$ inches to the right and left of the mid-sternal line, respectively; they do not change with posture. The heart's sounds at the apex are clear and show no alterations. There is a musical systolic murmur after the first sound, and it is transmitted to the left axilla. The aortic second sound is somewhat increased in intensity. A regular heart rhythm is interrupted by premature beats, which are fairly frequent; most of them reach the wrist. The arteries are thickened but not tortuous. The pulse is of good volume. The systolic blood pressure is 120 mm. Hg.

The upper level of liver dullness commences at the 7th rib; the lower limit is at the rib margin. Neither liver nor spleen is to be felt. There is no abdominal tenderness or other abnormality. The urine is normal. A Wassermann reaction is negative.

Observations upon the paroxysms.—Short paroxysms of tachycardia have been recorded upon almost all of the numerous occasions of examination. Nevertheless they are relatively infrequent; as a rule two or three paroxysms occur during the two or three hours of investigation. They last for a time varying from two or more seconds to an hour. The majority of the paroxysms last from 10 to 20 seconds. The patient is absolutely unconscious of onset and offset and is unaware of the paroxysm while it is present. Apart from posture, we have been unable to ascertain that any factor influences the presence or absence of paroxysms to any real extent; they appear to be more frequent in the standing and sitting postures.

With a solitary exception, an exception which will be described in detail, the recorded paroxysms have consisted of regular tachycardias, the rate rising from the normal of 80 or 90 beats per minute to 122 or 170 per minute. The usual paroxysmal rate is between 135 and 145 per minute. These paroxysms are due to new rhythms arising from an abnormal point in the auricle. On one occasion, after a prolonged period of regular tachycardia, the mechanism altered to fibrillation. The preceding regular tachycardia was the most rapid observed, namely 170 beats per minute. The rate during the fibrillation was variable, it rose at times to 190 beats per minute.

Description of the graphic records.—Examples of paroxysms as they appear in radial pulse curves are shown in Fig. 5 and 6. Fig. 6 shows a

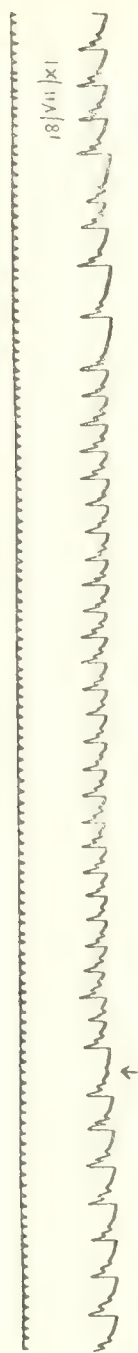


Fig. 5. CASE 2. A paroxysm of regular tachycardia taken on July the 18th, 1911. It lasts 14 seconds. The first beat of the paroxysm fails to affect the pulse. The paroxysm is followed by a long post-paroxysmal pause and a period of retarded pulse rate, which is interrupted by a single premature beat. The time marker in all sphygmographic curves is in 1.5 sec.

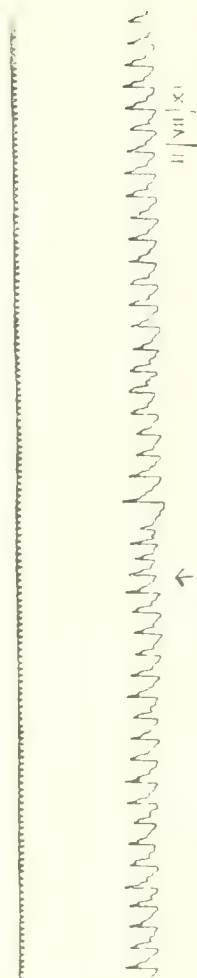


Fig. 6. CASE 2. A short paroxysm of 4 beats taken on July the 11th, 1911. The paroxysm starts abruptly and finishes equally suddenly. It is followed by a post paroxysmal pause and by a short period of pulse retardation.

paroxysm of 4 beats only. Fig. 5 is an example of a paroxysm of longer duration. Most of the paroxysms have been similar to that portrayed in this curve. The onset and offset are quite abrupt. The offset is marked by a considerable degree of pulse slowing which vanishes within a few cycles; this phenomenon has been observed in many previous cases. A single premature contraction interrupts the normal rhythm shortly after it is resumed (in Fig. 5).

The premature contractions which interrupt the slow rhythm are of four kinds. Very occasionally the points of origin lie in the ventricle. The electrocardiograms have shown that some of these premature ventricular beats arise in the left or apical portions of the ventricle, some in the right or basal portions of the ventricle; we do not consider it necessary to reproduce the figures. The majority of the premature beats have arisen in the auricle; and they originate in two auricular foci, both of which lie at a distance from the pacemaker. The two types are illustrated by Fig. 12 and 15. In Fig. 12 the normal rhythm, to which the first three and the last cycle belong, is interrupted by a single premature contraction, arising in the auricle and represented by *P*, *R* and *T* summits. The *R* and *T* summits of the premature beats are similar to those of the rhythmic beats. The *P* summit of the premature beat is partly iso-electric, but is mainly a deviation in the upward direction; it differs from the *P* summits of the rhythmic beats. The second type of premature auricular contraction is shown in Fig. 15. As in the first type, the ventricular complex is similar to that of the rhythmic beats. On the other hand, the auricular representative is of different form. It consists of a deviation in the downward direction.

The short and regular paroxysms, a very large number of which have been observed, have been of one type. They are illustrated by Fig. 13, 14 and 16. They consist of a succession of beats arising in the auricle at the same point from which the second type of single premature beat is shown to arise (Fig. 15). The centre of such a paroxysm is published in Fig. 13, in which the rate is approximately 140 per minute. The cycles consist of a downwardly directed auricular representative *P*, and the usual summits *R* and *T*, corresponding to the ventricle and of similar form to those of the rhythmic beats. The termination of a similar paroxysm is shown in Fig. 14. In a very large number of the observed paroxysms, single beats springing from the auricle, but arising in a focus which is distinct from that at which the usual paroxysmal beat originates and from that at which the rhythmic beat of the slow periods arises, interrupt the paroxysm itself. Two examples of this phenomenon are shown, namely, the last cycle but one in Fig. 13 and the last cycle of the paroxysm in Fig. 14. The majority of these interrupting beats are slightly premature in relationship to the rhythm of the paroxysm. This is shown in Fig. 14, but in Fig. 13, the interrupting beat falls at its proper time. A comparison of the interrupting beats with the premature beat of Fig. 12 shows that they arise from the same focus. It has been remarked that they frequently terminate a paroxysm.

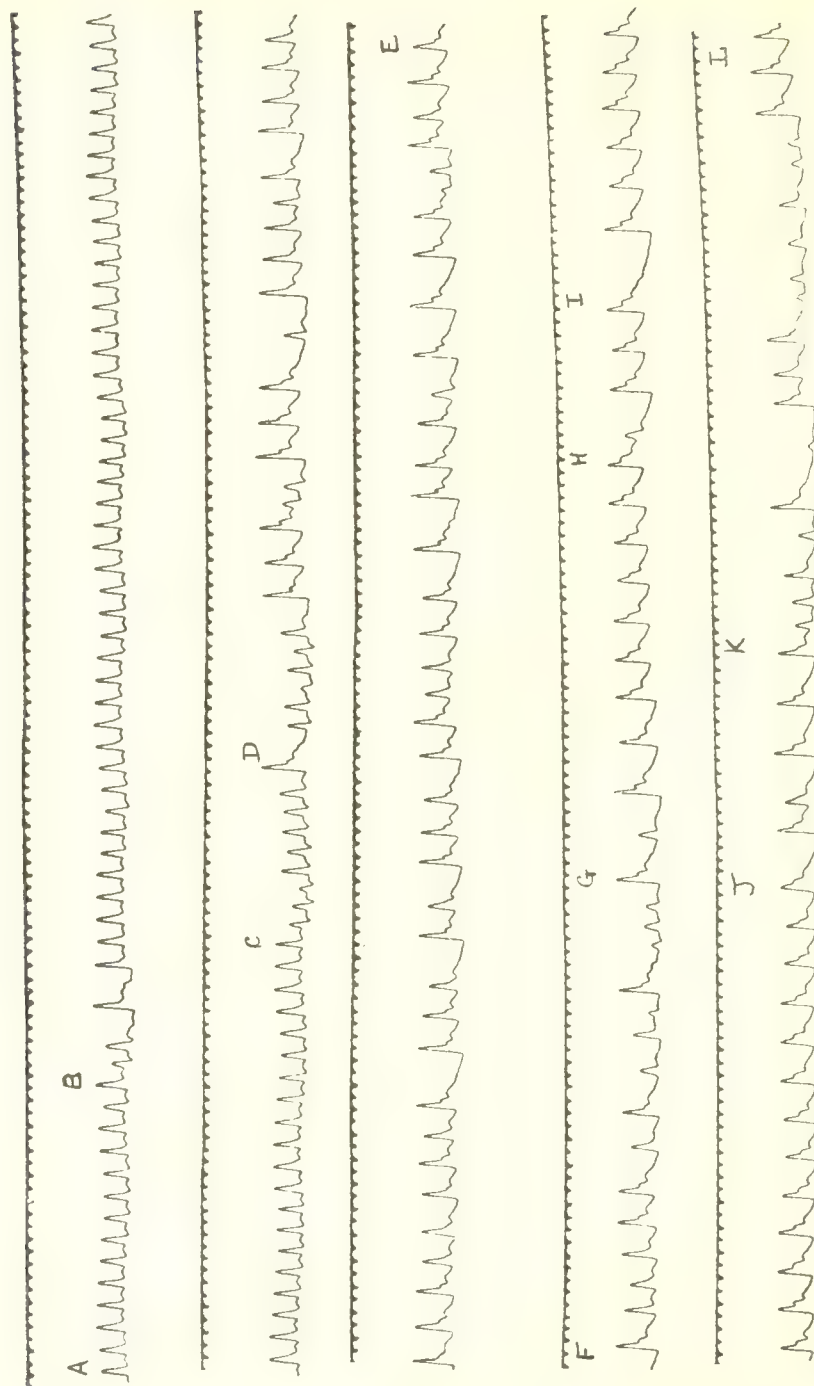


FIG. 7. *CASE 2.* Portions of a continuous sphygmographic curve taken from the radial artery on July the 18th, 1911. A regular paroxysm preceded it up to the point marked *A*; it is continued, with the exception of a short irregular period at *B*, up to *C*. At this point the pulse becomes irregular and at *D* the irregularity is complete. At *D* the auricle is fibrillating; the fibrillation is continued between *D* and *E*. Between *E* and *F* a portion of similar curve of 45 seconds duration has been excited. The fibrillation terminates at *G*, where the normal rhythm, interrupted by solitary premature beats, takes its place. Premature beats are seen at *H*, *I* and *J*. At *K* fibrillation sets in once more and the commencement of an attack of over one hour's duration is shown.

To sum up, the paroxysms consist of beats which arise in a single abnormal focus in the auricle and these abnormal or ectopic rhythms are disturbed by interruptions from a second ectopic focus. It is noteworthy that both the types of beat found during the paroxysms are also found as interruptions of the normal slow rhythm. Briefly, the patient possesses two foci of irritation in the auricle, each of which lies at a distance from the pacemaker. Both foci generate single new impulses and one of them generates impulses in succession.

We now pass to a description of certain events recorded on the 18th of July, 1911, and we may conveniently commence with a description of a continuous sphygmographic curve taken over a period of several hours on the afternoon of that day, (Fig. 7). When the patient first came under observation, the pulse was very irregular, but by the time the sphygmograph had been arranged, it was regular and beating at an approximate rate of 170 to 180 per minute. The patient exhibited a regular paroxysm of the usual form, though of somewhat faster rate. The regular paroxysm ran for 72 seconds, up to the point marked *A* in Fig. 7. At the point marked *B*, it became irregular for a second or more. The continuous curve is given in successive strips. At *C* the pulse shows some irregularity. At *D* it becomes very irregular and assumes the form which is so characteristic of auricular fibrillation. The same mechanism is continued from *D* to *E*; between *E* and *F* a portion of the curve of 45 seconds' duration and of precisely similar form has been excised. From *F* to *G* the fibrillation continues. At *G* the normal rhythm is resumed, but is interrupted by occasional premature beats at *H* and *I*. The normal rhythm is continued up to the point marked *J*. Occasional premature contractions then appear, and at *K* the complete irregularity, which is characteristic of a fibrillating auricle, commences again and continues to the end of the tracing (*L*). Following upon this strip, the completely irregular pulse continued for 69 minutes. The normal rhythm reappeared for 32 minutes. It was then interrupted by a paroxysm lasting 14 seconds. This paroxysm is shown in Fig. 5. A period of normal rhythm of 6 minutes' duration followed, and this in its turn was succeeded by a regular paroxysm of 21 seconds duration. The normal rhythm which followed was watched for 25 minutes, when the observations came to an end.

During the progress of the continuous radial curve, a large number of electrocardiograms were obtained. The first curve (Fig. 16) was taken somewhere between the points *A* and *D* in Fig. 7. The paroxysm consists of a succession of beats of a similar character to those shown in Fig. 9. The two curves differ mainly in rate. A second electrocardiogram (Fig. 17) was taken shortly after the onset of the complete irregularity (Fig. 7 *D*). Fig. 18 was taken during the stage of complete irregularity following *L* (Fig. 7).

The electrocardiograms, Fig. 17 and 18, testify conclusively to the presence of fibrillation of the auricles. The ventricular beats, represented by *R* and *T* summits of the usual form, are scattered throughout the curves

at irregular intervals. The summits *R* are separated by portions of curve which differ slightly from each other from cycle to cycle: this variation is due to the presence of the characteristic oscillations of auricular fibrillation, which are most marked in Fig. 18 (*f, f*).

In most instances of paroxysmal tachycardia arising in the auricle, whether the paroxysms originate in a single focus and are regular or whether the paroxysms originate in fibrillation and are irregular, it is noted that the height of the peak *R* during the paroxysmal stage is increased as compared with the normal. In the present case we have been unable definitely to ascertain the presence of this phenomenon, and probably this has been due in some measure to a phenomenon of an exceptional kind. In a number of radial curves obtained from the patient, very distinct evidence of a *pulsus alternans* has been obtained from time to time: and in electrocardiographic curves taken during the normal periods, a considerable variation in the amplitude of *R* has been frequently observed: this variation has not necessarily occurred in alternate fashion. This is well shown in Fig. 11, in which two *R* summits of large amplitude are followed by two *R* summits of lesser amplitude. Similar variations of amplitude have been frequently met with during the paroxysms. A notable example is shown in Fig. 13. A comparison of amplitudes during normal and paroxysmal periods has consequently been difficult or impossible.

DISCUSSION.

As we stated in our introductory remarks, the main object of this paper is to correlate two conditions, regular paroxysms of tachycardia arising in the auricle and auricular fibrillation. But while this is the main proposition before us, it is necessary to go somewhat further afield, and to collect certain accessory evidence bearing upon the production of pathological beats in the auricle. The view that tachycardia of auricular origin and auricular fibrillation have a common pathogenetic basis is but part of a more general conclusion. This general conclusion was dealt with by one of us at considerable length in a recent publication.¹⁰ The view is held in respect of both divisions of the heart, namely, auricle and ventricle: it is that there are three chief stages in the production of those pathological impulses which have been termed heterogenetic. There is the single and isolated heterogenetic impulse which gives rise to the simple premature contraction: there is the series of heterogenetic impulses giving rise to a new regular and fast rhythm; and, finally, there is the condition in which multiple foci are active and in which the musculature is so disturbed by impulses thrown out from multiple centres, that co-ordinate contraction is impossible and a state known as fibrillation ensues. The conception is that the three stages in the disorder of a division of the heart are due to a single underlying phenomenon, namely heterogenetic impulse formation. Variation in the degree of disorder is attributed to a variation in the degree of muscular

irritability in response to the exciting agent, or to a variation in the strength or distribution of the exciting agent. While the actual observations of this paper are more especially directed towards the proof of the close inter-relationship of new rhythms and fibrillation, it may be well to bring forward, in a general survey, the main facts upon which the general conclusion rests and to treat the special proposition of this communication as an integral part of it. The evidence is summed up in the following paragraphs.

1. When a weak faradic current is applied to the auricle or ventricle, and this current is gradually strengthened, a series of events is recorded. Single premature beats are first seen. An increase of current produces a regular tachycardia. Finally, with the strongest current, the muscle passes into fibrillation.

2. Many interferences with the muscle of the heart, as for example the administration of light percentages of chloroform or the injection of adrenalin⁴ or obstruction of the coronary vessels,⁶ awaken similar series of events. Single interruptions of the normal rhythm appear and these are succeeded by tachycardia and fibrillation, originating in the muscle affected.

3. A recent observation connects the tachycardias and fibrillation. It is well known that if an auricle be subjected to a fairly powerful faradic current and fibrillation is induced, it frequently happens that, at the cessation of stimulation, the fibrillation continues for some little while. The phenomenon is referred to by German writers by the apt term "*Nachflimmern*." We have observed the repeated replacement of this "*Nachflimmern*" by a regular tachycardia.

4. If a regular tachycardia is produced in the auricle by means of a weak faradic current, vagal stimulation will sometimes convert the tachycardia into auricular fibrillation.¹⁰

We may now sum up certain clinical evidence.

5. It is a usual experience in observations upon clinical cases of tachycardia of auricular or supraventricular* origin to find that the slow periods which separate the paroxysms are interrupted by premature beats of a precisely similar† nature. Our own observations include six cases, of which five have been previously recorded,^{5, 7, 8 and 9} and the second case of the present communication forms the sixth. Similar observations have been made by Cohn¹ and Laslett.³

6. Curves showing intermediate or transitional conditions between single premature contractions and long paroxysms of tachycardia are not

* We insert the word *supraventricular*, because in some of the cases it has been impossible definitely to establish the auricular origin of the paroxysm, although their generation in this division of the heart is probable in most of the instances referred to.

† Precisely similar in so far as the graphic methods employed are concerned.

infrequent in given cases. An example is shown in Fig. 5, where four premature beats follow each other in succession. Other examples might be referred to (Lewis,⁹ Cohn¹ and Laslett's² cases).

7. In patients who exhibit paroxysms of auricular fibrillation, the slow rhythm, which separates such paroxysms, is frequently interrupted by single premature auricular contractions. Two instances of this nature have come under the observation of one of us and have already been recorded.⁸ A series of similar cases was previously reported by Mackenzie.¹¹ An important instance of an allied type of case has been described by Hewlett,² a case in which certain transitions between the one form of irregularity and the other were observed.

8. Paroxysms of regular tachycardia of auricular or supraventricular origin and paroxysms of auricular fibrillation may occur in one and the same case. The writers have had an opportunity of studying a series of such cases and the two cases recorded in this paper are examples of this association. Moreover, the direct passage of regular paroxysms into fibrillation or fibrillation into regular paroxysms has been repeatedly observed. The original observation was made upon a case in which short paroxysms of regular tachycardia arising in the auricle interrupted the normal rhythm.⁸ On one occasion while electrocardiographic curves were being taken, the mechanism changed from tachycardia of auricular origin to auricular fibrillation, and subsequently the regular paroxysm was resumed. The same phenomenon probably occurred in Hewlett's case² (cp. Fig. 5 of his paper). It has also been recorded in a case described by Mackenzie¹² and in a case described by Turnbull;¹³ (in the latter the actual passage from one to the other was not caught). In the former the passage from one to the other was frequently caught. In the present paper, we have added two cases: in *CASE 1* a long paroxysm of many hours duration commenced as auricular fibrillation and terminated as a tachycardia of auricular origin. In *CASE 2*, a patient subject to numerous tachycardial paroxysms arising in the auricle, the passage of a paroxysm of this form into auricular fibrillation was observed and is shown in Fig. 7.*

9. The frequent association of auricular fibrillation with mitral stenosis and rheumatic heart disease is now a well recognised fact. In our own series, which comprises twelve cases of paroxysmal tachycardia of auricular or supraventricular origin, five were cases of mitral stenosis and in one of the remaining seven cases there was a history of rheumatic fever. We cite these figures for the purpose of showing that regular tachycardias and fibrillation are met with in a common class of cases.

While we divide heterogenetic impulse formation into three grades, the isolated premature beat, regular tachycardia and auricular fibrillation,

* Two new instances of the passage of regular paroxysms of tachycardia of auricular origin into auricular fibrillation have been observed by one of us, since these pages were written.

the division is an arbitrary one, and transitions from one stage to another occur and have been already referred to. Hewlett's case is a notable instance. *CASES 1* and *2* of the present communication may also be cited in this connection. In *CASE 1*, the regular paroxysm was interrupted by premature beats, which presumably were also of auricular origin, although they were not recorded electrocardiographically. *CASE 2* provides a clear instance of the transition. Paroxysms of regular tachycardia, generated in an ectopic focus, are interrupted by single beats, most of them premature in relationship to the paroxysm itself, springing from a separate ectopic focus. The presence of two active extraneous foci of impulse formation in the auricle, and the ultimate passage of a paroxysm into fibrillation in this patient, has a peculiarly significant bearing upon the question of the production of auricular fibrillation from multiple auricular foci. Whether the short period of irregularity recorded in Fig. 7 (at the point *B*) is a further transition or not we are unable to ascertain positively in the absence of the corresponding electrocardiogram, but we believe this to be the case.

We may sum up the previous discussion in the statement that there is a rapid accumulation of evidence, which shows the close association of the modes of genesis of three forms of disturbance of the normal cardiac rhythm, namely, premature contractions, paroxysms of regular tachycardia and fibrillation. The hypothesis represents the relation in more tangible form: the three forms of disturbance may be regarded as the expression of heterogenetic or pathological impulse formation of three grades, the production of single and isolated impulses, the occurrence of a series of impulses from a single focus and finally the activity of a number of such foci.

It is perfectly true that certain cases show one or other mechanism alone. It is also true that the connecting links in the individual case are often imperfect or absent: thus, cases of auricular fibrillation may apparently show intervening periods of slow and normal heart action which are perfectly regular. It is possible, nay probable, that records of the actual passage of normal mechanism to fibrillation in these last cases will ultimately reveal transitions, but we freely admit the possibility that such transitional curves may not occur, and that the changes may be abrupt from one to the other. An abrupt change from auricular fibrillation to a normal mechanism is indeed the rule in experiments upon healthy hearts, but we cannot see that these observations appreciably affect our general contention.

SUMMARY.

1. Two instances of paroxysmal tachycardia are recorded. In the first case, the paroxysms usually consisted of auricular fibrillation: on one occasion, at least, the passage of the fibrillation into a regular tachycardia

of ectopic auricular origin was observed. In the other instance, the paroxysms consisted of tachycardia of ectopic auricular origin: on one occasion the passage of such a tachycardia into fibrillation and the subsequent resumption of the normal rhythm, interrupted by regular paroxysms, was observed.

2. The regular tachycardias in these two cases were interrupted by premature contractions, which in one case probably, and in the other case certainly, came from a separate and ectopic auricular focus. The significance of this observation and its relation to the passing of regular tachycardia into fibrillation is discussed.

3. A detailed account of the evidence, which leads us to the view that the single premature contraction, ectopic tachycardia and fibrillation have a similar pathogenesis, is given.

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- ⁶ LEWIS. *Heart*, 1909, I, 98.
- ⁷ LEWIS. *Heart*, 1909, I, 262.
- ⁸ LEWIS. *Heart*, 1910, I, 306, (Case 10, 11 and 15, and Fig. 9).
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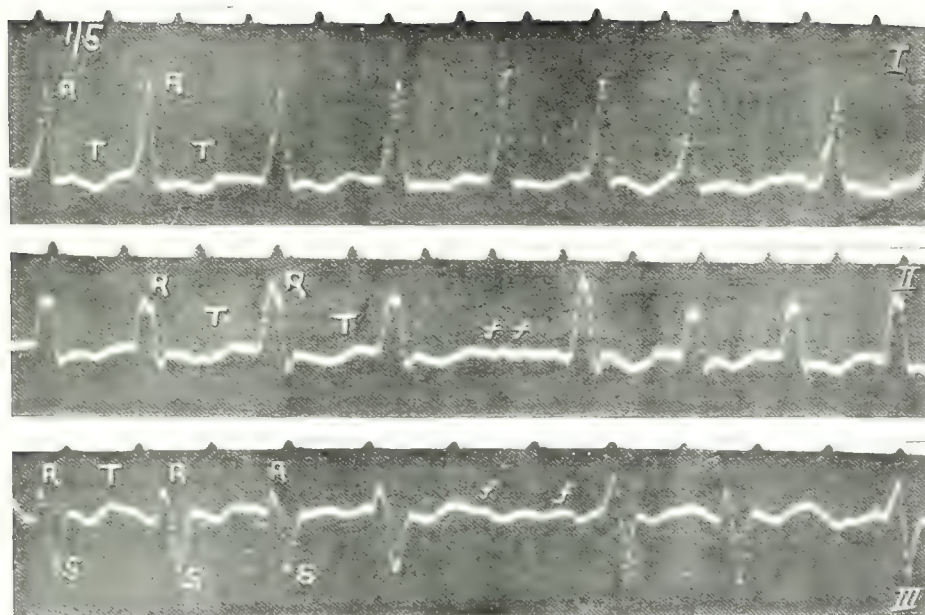


FIG. 10

1. The first tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

2. The second tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

3. The third tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

4. The fourth tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

5. The fifth tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

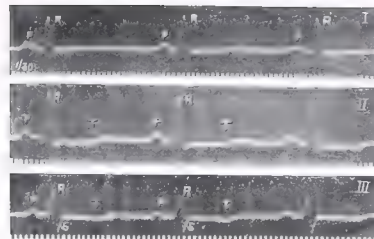
6. The sixth tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

7. The seventh tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

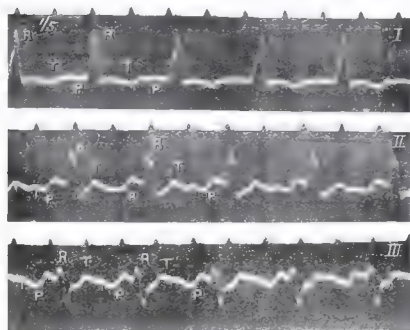
8. The eighth tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

9. The ninth tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.

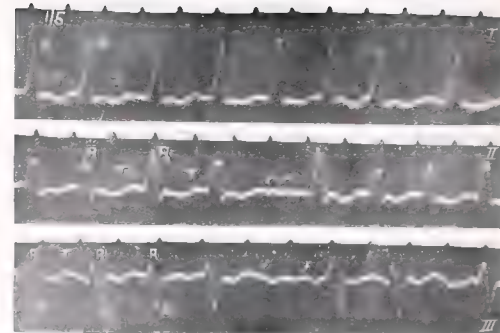
10. The tenth tracing shows a normal sinus rhythm with a rate of 70 beats per minute. The P waves are upright in leads I, II, and III, and the QRS complex is narrow. The T waves are upright in leads I, II, and III.



I



II



III

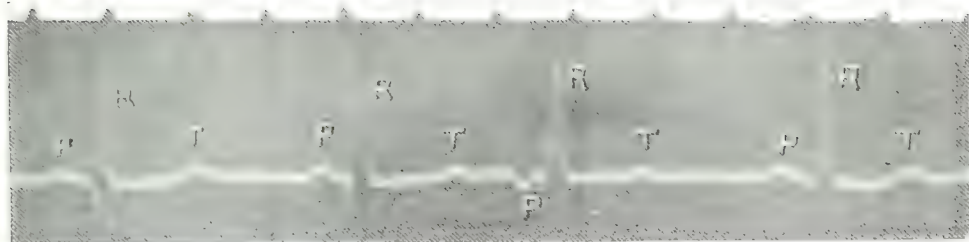


FIG 15

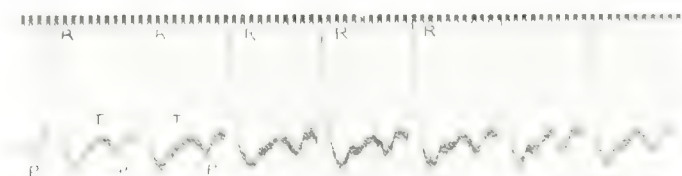


FIG 16.

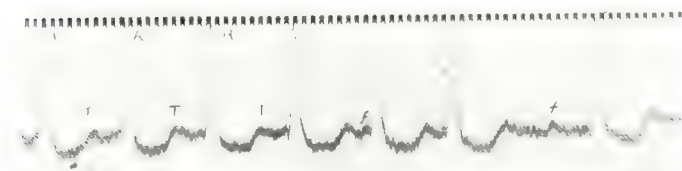


FIG 17.

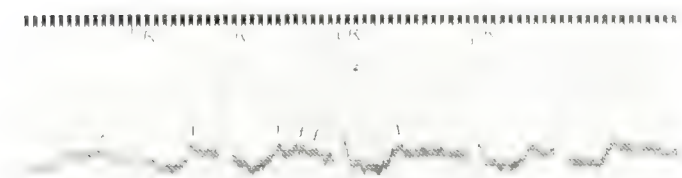


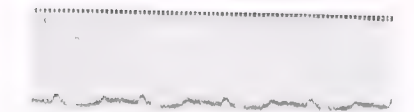
FIG 18

$$T_{\text{max}} = \frac{\pi}{2} + \frac{\pi}{2} = \pi$$

For $\alpha \in \mathbb{R}$, let \mathcal{P}_α denote the set of all probability distributions P on \mathcal{X} such that $\int_{\mathcal{X}} x dP = \alpha$. Let \mathcal{P}_α^0 denote the set of all probability distributions P on \mathcal{X} such that $\int_{\mathcal{X}} x dP = \alpha$ and P is absolutely continuous with respect to the Lebesgue measure.

1. *Chlorophyll a* and *Chlorophyll b* were determined by the method of Lichtenthaler and Whistler (1972). The *Chlorophyll a* and *Chlorophyll b* contents were expressed as mg g⁻¹ of fresh weight.

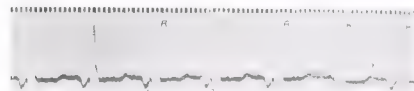
The time marker is at 1.5 sec.

[illegible]
$$S_{\text{eff}} = \int d^4x \sqrt{-g} \left[\frac{1}{2} R - \frac{1}{2} (\partial_\mu \phi)^2 - V(\phi) \right] + \int d^4x \sqrt{-g} \mathcal{L}_m$$


1 2 1



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5



PAROXYSMAL TACHYCARDIA ACCOMPANIED BY THE VENTRICULAR FORM OF VENOUS PULSE.

By C. D. S. AGASSIZ.

(*From the City of London Hospital for Diseases of the Chest*).

A. S., a man aged 55, was admitted to the City of London Hospital for Diseases of the Chest on June the 8th, 1911, complaining of cough, shortness of breath and pains in the chest and shoulders.

Notes on admission.

Family history. His father died of a "paralytic" stroke. His mother died of cancer of the breast. A brother died of "heart trouble" and a daughter has "mitral stenosis." Two other brothers and four sisters are dead, but there is no history as to the cause of death in any of them. One brother is alive and well.

Previous illness. As a child he had measles. 26 years ago he had an attack of acute rheumatism for which he was treated in hospital for three weeks. A fortnight after his discharge he had a relapse and consequently returned to hospital for another 16 weeks. He has had influenza from time to time and states that he has suffered at intervals during the last 26 years from similar symptoms to the present ones. He denies ever having had syphilis, but his blood has given a positive reaction to the Wassermann test.

Present illness. The present attacks began four weeks before admission, when shortness of breath, swelling of the feet and puffiness of the eyes were noticed.

Condition on admission to hospital. The pulse rate is 160 and the respirations 40 to the minute. There is extensive pulsation of the veins of the neck, easily palpable and forcible when the patient stands. The systolic blood pressure is 165 mm. Hg. (Riva-Rocci). Considerable cyanosis of his lips and ears and dyspnoea, which becomes urgent when the patient lies down, are present. The arteries at the wrist are considerably thickened. The apex beat is palpable in the fifth left interspace. The cardiac dulness extends $2\frac{1}{2}$ and 7 inches to right and left of the mid-sternum. A soft systolic murmur is heard at the apex, the second sound is scarcely audible. A well marked systolic murmur is heard at the aortic area and the second sound is not distinct. The pulmonary and tricuspid sounds are almost inaudible. There are numerous râles over the bases of both lungs and universal wheezing inspiratory and expiratory rhonchi. Signs of ascites are found and the liver, which is palpable three fingerbreadths below the costal margin, shows pulsation. There is cedema of the feet and legs. The urine is scanty in amount; it contains a trace of albumen and hyaline and granular casts in the deposit.

Frequency and duration of paroxysms.

When the patient first came under observation he was in a paroxysm which continued without break for a whole hour of observation. From June the 13th until August the 24th the pulse rate was fast on all the numerous occasions on which it was examined: but the tachycardia was interrupted from time to time by short periods of a slower and more normal rhythm; thus a short period of tachycardia generally lasted for from five to ten minutes and was usually followed by one or two beats, or a somewhat longer period, of the normal rhythm: on rarer occasions it was succeeded by a longer slow

period with a duration of perhaps as much as five minutes. The tachycardia was then resumed. The mechanism and its changes, as portrayed by polygraphic curves, is shown in Fig. 1 and 4. In Fig. 1 a prolonged paroxysm is interrupted by a slow period consisting of nine beats. In Fig. 4 a similar paroxysm ends in a post-paroxysmal pause, a single beat of normal rhythm follows, and the paroxysm is then continued. During the observations made between August the 24th and September the 1st the normal mechanism was usually present and only occasional paroxysms were seen. From September the 1st till the date of writing (October the 25th), no further paroxysms have been observed.

Interpretation of graphic records.

Mechanism of the heart during the slow periods.—The rate of the heart-beat during the slow periods has varied between 60 and 85 beats per minute. The rhythm was regular except for the occasional occurrence of premature contractions, which were of two forms, being usually auricular but occasionally ventricular. An example of the curves obtained during the slow periods is shown in Fig. 2. The *a* wave is small, the *c* and *r* waves prominent. The pulsation was so great during the ventricular portion of each cycle that the receiver was usually placed so that only one portion of the cup lay in contact with the pulsating area. The *a-c* interval over the period of observation has been almost constantly prolonged to 1½ sec. On a single occasion further evidence of heart-block was obtained during the slow period. This is shown in Fig. 7 in which a dropped beat occurs. The *a* waves in this figure are indistinct and the *a* wave belonging to the centre of the pause is not perceived. Nevertheless the length of the pause and the position of the remaining *a* waves leaves little doubt of the presence of a dropped beat. Alternation was present in the curves of the slow period from time to time. On one or two occasions it persisted for a number of cycles but more often it was only noticeable as a sequel to premature contractions. This is well shown in Fig. 3.

The electrocardiograms taken during the slow periods are shown in Fig. 8. Fig. 8 consists of three strips (*I*, *II* and *III*), which correspond to the three customary leads, *i.e.*, right arm to left arm, right arm to left leg, and left arm to left leg. Each strip shows two cycles, composed of an auricular event *P* and ventricular events *R, S, T* or *Q, R, S, T*. The *P* variations in lead *I* are inconspicuous. In leads *II* and *III* they are prominent. The *P-R* interval measures 0.27 seconds, as opposed to 0.12-0.17 seconds, the normal length. The shape of the ventricular complexes will be referred to again in discussing the paroxysmal curves.

Mechanism of the heart during the fast periods.—The heart rate during the paroxysms has varied considerably. When the patient was first seen the rate was 160 per minute, the highest limit reached; the lowest rate was 113 per minute; the usual rate was 125-130 per minute. There was no

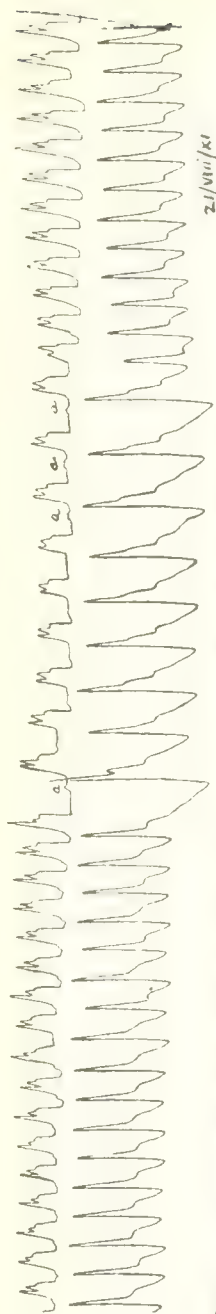


Fig. 1. A polygraphic curve showing the end of one paroxysm and the commencement of the next. The paroxysm ends in a post-paroxysmal pause. Alternation is present both during the paroxysm and during the normal period. It is more conspicuous at the onset than at the offset of the paroxysm. In all the polygraphic curves the time marker shows fifty seconds.

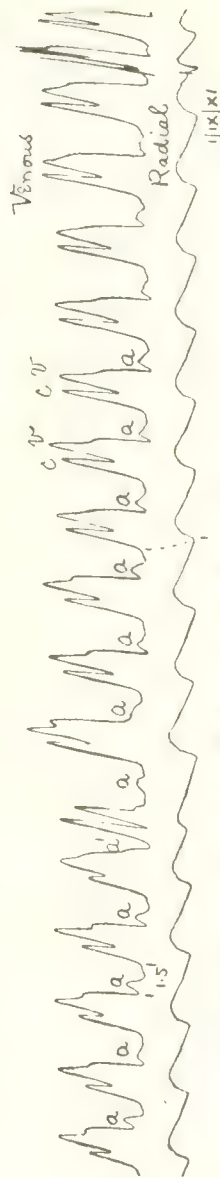


Fig. 2. A polygraphic curve taken during a slow period, showing the *a* waves and the prolongation of the *a-c* interval. A single premature contraction occurs; it has arisen in the atrium, as indicated by the shortness of the pause and by the presence of the little *a* wave, in the jugular pulse.

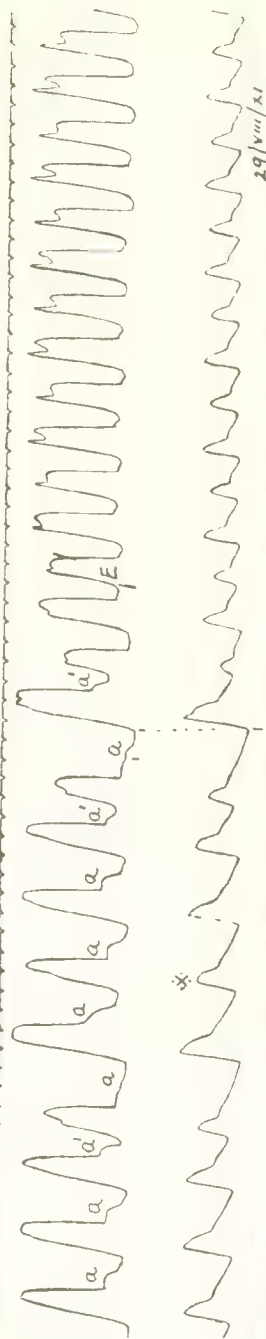


Fig. 3. The commencement of a paroxysm. The curve shows the *a* waves of the slow period, which is interrupted by two premature contractions of atrial origin (*a* waves). It also shows alternation following the first of these premature contractions. The small foot is marked by an asterisk. The paroxysm commences in a premature contraction, at which the *a'* wave is just visible in the venous curve. The paroxysm is continued and alternation is clear. The venous pulse is of the ventricular type throughout and the separate ventricular waves show alternation which is parallel to that of the radial curve.

change of rate on altering the posture of the patient (lying, sitting or standing) on any of the numerous occasions upon which he was tested in this manner. The jugular curves of the paroxysms are illustrated by Fig. 1, 3, 4 and 6. They are of the ventricular form: no sign of an *a* wave is discovered during the periods of tachycardia. The venous pulse shown in Fig. 3 is of the plateau form, with sharp upstroke and downstroke at the beginning and end of the ventricular systole respectively (period marked *E*). Occasional premature beats interrupted the paroxysms, one such is shown in Fig. 5. Alternation during the paroxysms was common and was especially prominent after premature beats (Fig. 5) and at the commencement of paroxysms (Fig. 1, 3 and 4). Alternation also occurred in the venous curve, as shown in Fig. 3.

The electrocardiograms of the paroxysmal period are shown in Fig. 9. In all the electrocardiograms the ordinates represent 10^{-4} volts. This figure consists of strips *I*, *II* and *III*, and they are from the corresponding leads. A comparison may be instituted between the shape of the ventricular complexes of these three strips and those of the slow rhythm (Fig. 8). In lead *I* of Fig. 8, *R*, *S* and *T* variations are present and *T* is upright; in lead *I* of Fig. 9 *T* is partially inverted; the measurements of *R* and *S* in Fig. 8, *I*, and Fig. 9, *I*, show no appreciable differences. In lead *II* of Fig. 8 ventricular systole is represented by *Q*, *R* and *S* and an upright *T* variation; in Fig. 9, *II*, it is represented by similar variations except that *T* is again partially inverted. In Fig. 8, *III*, *Q*, *R*, *S* and *T* variations are present; in Fig. 9, *III*, these same variations are seen, but *S* is much deeper and *T* is once more partially inverted. The slight irregularities of this curve (Fig. 9, *III*) are due to muscular tremor.

The first noteworthy feature in regard to these curves is the similarity of the electric variations which correspond to the opening phases of ventricular systole during slow and fast periods. It is taken as evidence of the supraventricular origin of the paroxysms. The partial inversion of *T* in the paroxysmal curves is not opposed to this view, for such a modification is well known to accompany a change of heart rate. The second feature of the paroxysmal curves, to which attention is drawn, is the absence of a recognisable variation *P*, the auricular representative. Now these features are both frequent in cases of paroxysmal tachycardia, in which the ventricular form of venous pulse is present, and amongst other causes they have been ascribed to the origin of such paroxysms in a point of the auricular tissue which gives an auricular representative of an anomalous form and one which is in consequence difficult to identify. The explanation of the absence of a wave in the jugular curves and the difficulty of identifying *P* variations in isolated paroxysmal curves will be more readily appreciated when the curves which show the onsets of paroxysms are considered.

Mechanism of the transition.—In cases of paroxysmal tachycardia it is often necessary to obtain the complete series of graphic records, namely the

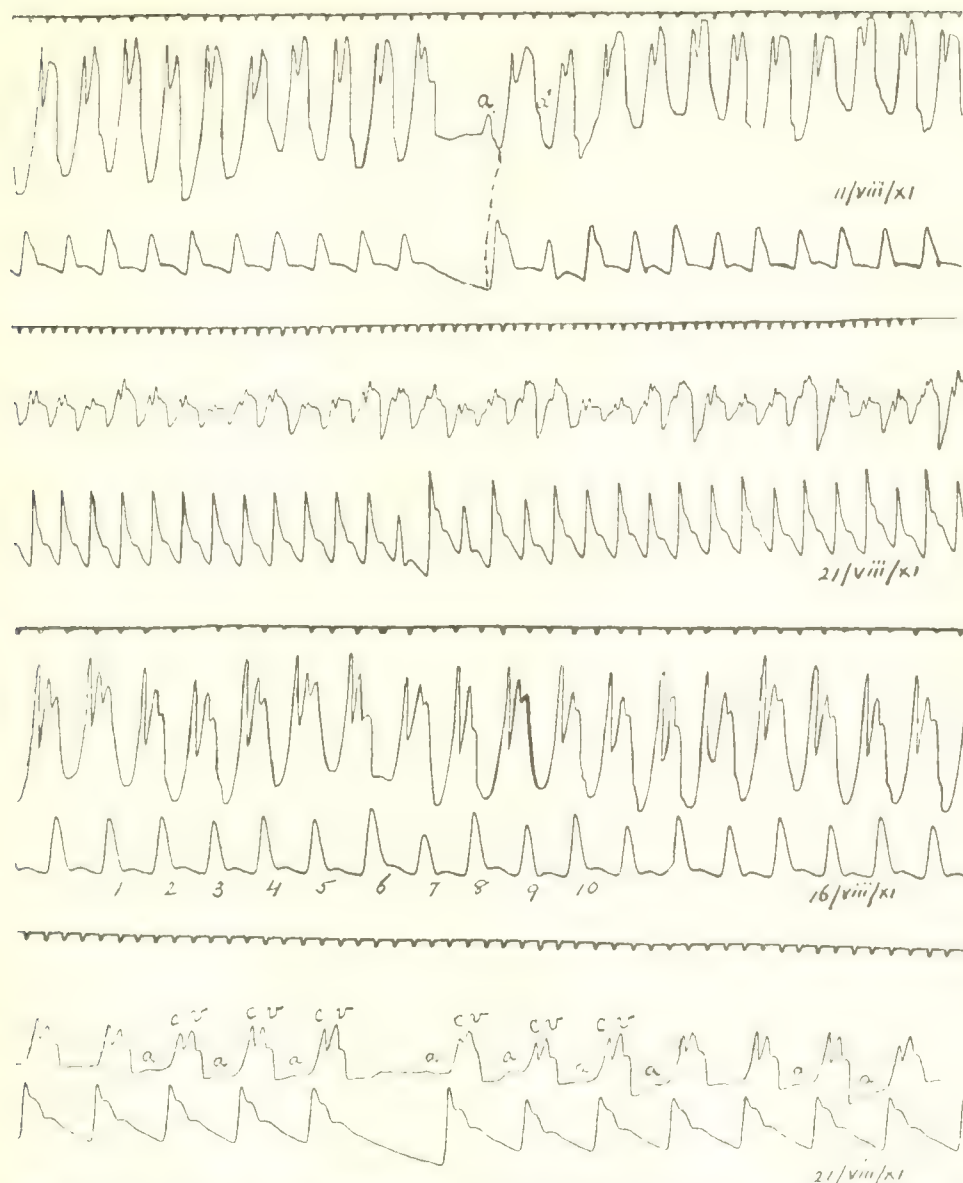


Fig. 4 shows the end of one paroxysm and the beginning of another. The post-paroxysmal pause and a single beat of the normal rhythm separate the two paroxysms. The only auricular representatives found in the curve are those which precede the normal beat and that which precedes the first premature radial beat at the commencement of the paroxysm.

Fig. 5 shows the interruption of the paroxysm by a premature contraction which is followed by alternation.

Fig. 6. A polygraphic curve from the paroxysmal period, showing an increase in the degree of alternation. Slight alternation is present in beats 1-5, beat 6 shows an abrupt exaggeration and is followed, in beats 7-10, by an increase in the degree of alternation.

Fig. 7. A polygraphic curve from the slow period, showing a single dropped beat.

venous curves of the normal and paroxysmal period and the two series of electrocardiograms, each from three leads. But occasionally even this evidence is insufficient in obtaining a complete analysis of the mechanism which is present. Very considerable help is always obtained in such cases by a consideration of the curves taken at the transition from paroxysm to slow rhythm and slow rhythm to paroxysm. The polygraphic curves Fig. 3 and 4 show the onset of paroxysms. Each begins with a premature contraction of the heart which is repeated, yielding a succession of rapid beats. The paroxysms end in long pauses (Fig. 1 and 4), which are similar in duration to the pauses which follow the premature auricular contractions interrupting the slow periods. These facts suggest the origin of the paroxysms in the auricle. The same origin is evidenced, as we have seen, by the nature of the ventricular complexes in the electrocardiographic curves; for from these it may be concluded that the paroxysms arise in a supraventricular focus. As a matter of fact the position of the first beat in each paroxysm (Fig. 3 and 4) is such that the auricular contraction is recognisable (marked *a'* in Fig. 3 and 4); but after the first beat, when the heart cycles follow more closely upon each other, the *a* waves are no longer visible. Precisely similar events are to be found in the electrocardiographic curves which correspond to the passage from slow to fast period (Fig. 10 and 11 are illustrative of this point).

Fig. 10 commences with a cycle of the slow period and is represented by *P*, *Q*, *R*, *S* and *T* variations. This cycle is of considerable importance because, belonging as it does to the slow period, the shape of *T* is known. (The curves may be compared with Fig. 8, *III*). There is a noticeable difference between the shape of this *T* variation and those of Fig. 8, *II*, and the difference is due to the superimposition of an anomalous *P* summit upon the *T* variation in question.* The next ventricular cycle of the same figure is a response to the premature contraction of the auricle but, as the pause which precedes it is relatively short, the *T* variation which belongs to it is partially inverted. The second premature auricular contraction of the series is obscure, for we have no uncomplicated ventricular cycle of the same type to compare with it. Had we a record of the last beat, such a comparison would have been possible, but unfortunately the terminations of paroxysms were not obtainable. Precisely similar events are shown in Fig. 11. Here the last two beats of the slow period are shown, and also the first beat of a commencing paroxysm. The two slow cycles are represented by *P*, *Q*, *R*, *S* and *T* variations of similar form, except that the second *T* is modified by the usual superimposition of an anomalous *P*. Thus the commencements of the paroxysm demonstrate that the tachycardia is auricular in origin, and in view of the fact that the *P* variations, visible at the onsets, are obviously not of precisely the same form as the *P* variations of the slow rhythm, the point of origin of the paroxysms, though auricular, is known to lie at a distance from

* The difference is slight, though distinct, in the reproduction, which is reduced; is quite clear in the original curve and constant through a series of curves.

the pacemaker of the heart. We are dealing consequently with paroxysms of ectopic and auricular origin. That the paroxysm arises from a single auricular focus is recognised from its regular sequence of beats and from analogy with other cases. The absolute position of auricular representatives in the centres of the paroxysms is not known, but, from a comparison of the *P-R* intervals in such an example as Fig. 10, it is apparent that the third *P* falls somewhere during the progress of the *T* variation. Auricle and ventricle contract simultaneously throughout; the auricular contraction which falls with one ventricular cycle provides the impulse for the succeeding ventricular contraction. The synchronous contraction of auricle and ventricle results in this case from prolongation of the *As-Vs* interval (*a-c* or *P-R* in the figures); a prolongation which is evident during the slow periods and at the commencement of each paroxysm. We have therefore a ready explanation of the absence of *a* waves from the jugular curves during the paroxysmal stage; *a* and *v* are falling together.

The electrocardiographic curves of the slow periods occasionally showed premature contractions. They were precisely similar in form to the first beats of the paroxysms as they are illustrated in Fig. 10 and 11.

In describing the polygraphic curves of paroxysms, certain early contractions were noted (Fig. 5). The only instance in which such an early beat has been recorded electrocardiographically proved that it arose in the ventricle. At the end of Fig. 10 a large downward variation is succeeded by an upward variation, a diphasic curve, which is usually held to indicate the origin of the corresponding contraction in the apical or left portions of the ventricular muscle.

In the polygraphic curves, the frequent occurrence of a premature contraction as the last beat of a paroxysm has been remarkable. The same event has often been seen but has not been recorded electrocardiographically. The premature beats were of ventricular form as shown in Fig. 10. The occurrence of premature beats at the end of paroxysms has been so frequent that it cannot be attributed to coincidence but must have had some definite relation to the actual termination. During the paroxysms they have been comparatively rare; thus, in records of 46 paroxysms a premature contraction ended the tachycardia in 19 instances, while only 6 premature beats were found buried in the same paroxysms.

CONCLUSIONS.

The observations upon this case are of importance because they help to elucidate an obscure form of paroxysmal tachycardia. It is shown that in a patient, in whom regular paroxysms of tachycardia were accompanied by the ventricular form of venous pulse, the paroxysms were of auricular origin and that the purely ventricular outline of the jugular pulsation, and the absence of sign of an *a* wave, resulted from synchronous contraction of

auricle and ventricle ; it is also shown that the synchronism of contraction was due to a delay in conduction and the consequent coincidence of an auricular contraction with the preceding ventricular cycle.

While this was certainly the mechanism in the instance described, it does not necessarily follow that a precisely similar mechanism occurs in other cases of paroxysmal tachycardia accompanied by the ventricular form of venous pulse ; in fact, this is probably not the case. At the same time we now have evidence of one of the ways in which such paroxysms are produced.

I take this opportunity of expressing my indebtedness to Dr. Thomas Lewis for the electrocardiograms and for his aid in their interpretation.

I am indebted to Dr. W. J. Hadley for permission to publish the clinical notes of the case.

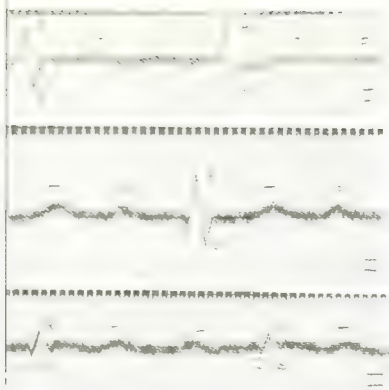


FIG. 8.

8. Three electrocardiograms from the slow per
III respectively, and correspond to the three
interval is prolonged in each curve. All the
the horizontal lines are separated by the values
s in thirtieths of seconds in all the electrocard

9. The three corresponding leads taken during
complexes are of the same form as presented
representatives are not apparent

10. shows the end of the slow period and the
cycle of the figure, with its accompanying *P* and
The *T* summit of this cycle has a *P* summit
premature contraction, the first beat of the par
a semi inverted *T* summit and consequently it
falls with it. The three succeeding cycles are
a premature beat, arising in the ventricle, into

11. shows the two last beats of a slow period and
of the second beat of the slow rhythm is complete
variation (*P*) and this *P* belongs to the first cycle

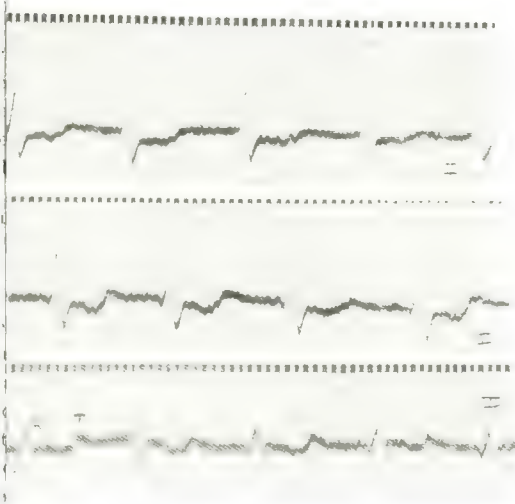


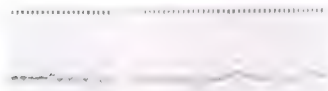
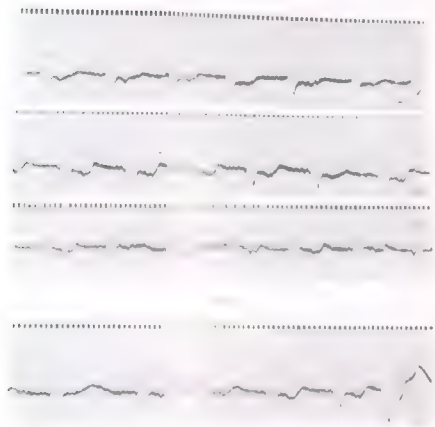
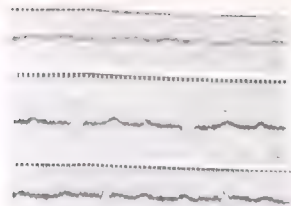
FIG. 9



FIG. 10



FIG. 11



ACUTE CARDITIS AND HEART-BLOCK.

By H. G. BUTTERFIELD.

(*University College Hospital Medical School*).

F. K., girl aged 16 years, was admitted to the City of London Hospital for Diseases of the Chest on May the 26th, 1911.

History. There was no history of heart disease or of rheumatic fever in the family. The patient contracted measles in infancy and had suffered from time to time with pain between the shoulders. There was no history of acute rheumatism, scarlet fever, whooping cough, pneumonia or chorea.

Five weeks before admission she complained of palpitation, pain in the chest and back after food, and pain in the knees.

She attended the Out-Patient Department for two weeks. On May the 12th, Dr. Riviere found that the heart was dilated and observed a systolic murmur of mitral origin. He advised the mother to leave the girl in the hospital.

She was finally persuaded to come into the hospital on May the 26th as the symptoms had become more marked. The patient was now seriously ill with pain in the left side, sleeplessness and shortness of breath. There had been cough and expectoration for one week.

State on admission.—The patient was anæmic, the tongue was slightly coated. The pulse rate was rapid, 132 per minute, regular and dicrotic. The heart's apex beat was in the fifth space, one inch external to the nipple line. There was a large extension of dulness to the right of the sternum. A systolic murmur was present at the apex, and over the sternum a well marked pericardial rub was heard. There were also friction sounds over the bases of both lungs at the back. In the same situation flatness of the percussion note was present. The urine was normal.

On the 27th the condition remained unaltered; the pulse was rapid, but the mechanism of the heart was normal (Fig. 1).

On May the 28th, some cyanosis was noted; the respirations had increased from 24 to 28 per minute and were embarrassed. The left border of dulness was then two inches outside the nipple line, the upper border was at the upper border of the third rib. There were loud systolic and rumbling diastolic bruits in the mitral area, the aortic sound was only faintly heard. The pulmonary and tricuspid sounds were normal. The friction was still present. There was bronchial breathing at the right apex, moist crepitations at both apices and well marked dulness over both bases, more especially over the right. Breath sounds over the right base were almost completely absent. Rales were heard on both sides.

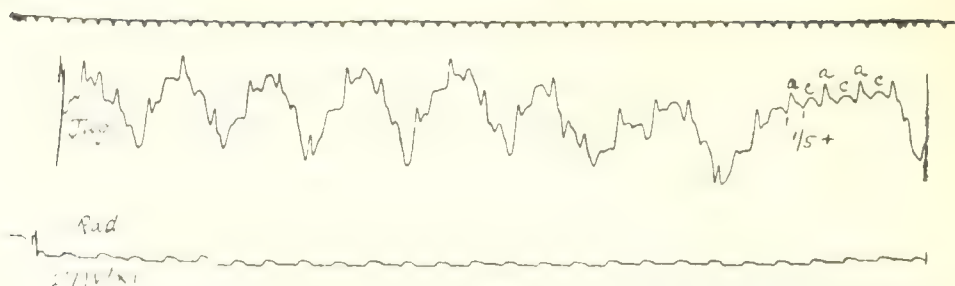


Fig. 1. A polygraphic curve taken on May the 27th. The radial pulse is rapid and irregular. The jugular curve shows marked respiratory excursions, except at the end of the tracing, where breathing ceased. The *a* waves are clear for three cycles and the *a-c* interval slightly exceeds one fifth of a second.

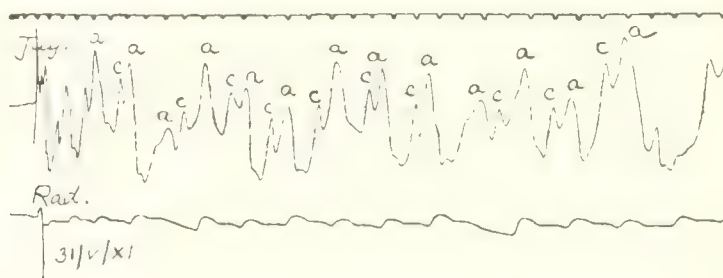


Fig. 2. A polygraphic curve showing two dropped beats. The *a-c* intervals show progressive increase up to the point at which these beats are dropped. The longest interval is approximately $\frac{1}{3}$ second. (May the 31st.)

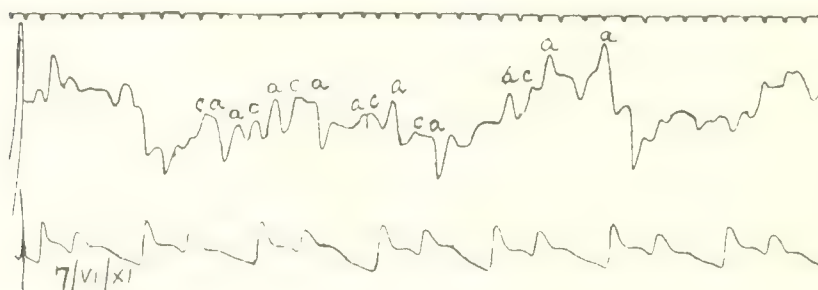


Fig. 3. A polygraphic curve taken on June the 7th. A ventricular response is lost after each third auricular contraction.

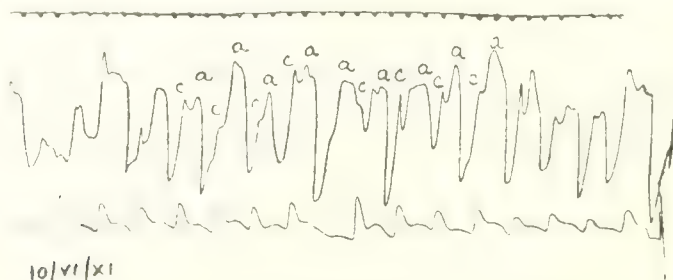


Fig. 4. A polygraphic curve taken on the day of death. It shows occasional dropped beats. (June the 10th.)

On May the 30th, the pulse was first noticed to be irregular; the irregularity was due to partial heart block, and consisted of occasional pulse intermissions.

On May the 31st, the blocked beats were still present (Fig. 2). The physical signs in the chest remained practically unaltered.

On June the 1st she received digitalis in 10 minim doses of the tincture and this was continued until June the 5th. Dropped beats were present throughout the whole of this time and the patient showed considerable improvement, in so far as her symptoms were concerned, up till the day on which the digitalis was discontinued, when she became more dyspnoëic and cyanosed.

On June the 7th, one beat in three was missed (Fig. 3), and on the 8th, a pause occurred after each third or fourth beat; on these days, tubular breathing was heard in the right axillary region. Pericardial friction was still present, but was not so audible.

During the stay of the patient in hospital, the temperature was intermittent, ranging from 97-100 degrees Fahrenheit. The pulse rate varied from 80-136; the respirations from 24 to 48. The urine flow was plentiful throughout.

The dropped beats continued till the time of death (Fig. 4), which occurred on June the 10th at 6.15 p.m. The post-mortem was held at 2.30 p.m. on the 12th.

Post-mortem.

The body is that of a well nourished girl. The œsophagus and trachea, the cervical and bronchial glands appear healthy. In the right pleural sac there is a quantity of clear yellow fluid; a little is also seen in the left cavity. The lungs (right, 17 oz., and left, 15 oz.) are somewhat œdematous and there are patches of collapse in the right organ. The pericardium is loosely adherent; recent adhesions, readily separated, are present, and there is no excess of fluid. The epicardium is covered with a semiplastic exudate.

Heart.—The weight with the pericardium is 22 oz.; the weight without the pericardium 15½ oz.. The muscle is soft, friable and pale. There is no evidence of fatty change. The left ventricle is markedly dilated. The mitral valve exhibits a series of recent vegetations near the flap margins. The ring is not narrowed. The aortic valve is studded with small recent vegetations along the borders of the cusps. The valve is incompetent. The right ventricle shows dilatation. There are a few fresh vegetations on the tricuspid valve margins, and there is an extensive accumulation of ante-mortem clot around the valve curtains. The pulmonary valves are healthy.

The liver weighs 57 oz., and is engorged. The kidneys weigh 8½ oz. together and have a healthy appearance. So also has the spleen, which weighs 6½ oz.. The remaining abdominal organs are normal. No secondary abscesses are to be found.

Microscopic examination of the heart.

The heart had been fixed in Formol-Muller solution. This was washed out as far as possible and the remainder of the fixation carried out in a solution of four per cent. formalin in normal saline. The area containing the auriculo-ventricular node and bundle was excised. All were hardened and dehydrated in absolute alcohol, passed through carbon bisulphide and thence embedded in paraffin with a melting point of 52° Centigrade. Two pieces of tissue were removed from the centre of the external wall of each of the chambers of the heart, in planes parallel and at right angles to the surface. Portions of the valves and the thickened pericardium were also taken. The sections of the node and bundle were cut in series, every fifth being mounted. The sections were cut 12 micromillimetres in thickness, with an occasional thin one at regular intervals to obtain minute histological detail, and were stained with Ehrlich's acid hæmatoxylin and van Gieson's solution; the sections from the remaining blocks of tissue were of varying thickness and were stained with hæmatoxylin and eosin, hæmatoxylin and van Gieson's solution, the methyl green and pyronin mixture of Pappenheim and Mann's methyl-blue eosin mixture. The bacteriology was studied mainly in the valves, the methods used being the Eosin-Gram-Weigert procedure for the Gram staining organisms and Zieler's method for the bacteria in general.

Frozen sections were also cut from various parts of the heart and stained for fat with Scharlach R in acetone-alcohol solution, control tissues known to be fatty being used in all cases to verify the staining properties of the reagent. Repeated attempts to demonstrate fatty particles in the muscle fibres had negative results.

Bacteriological examination showed the presence of numerous Gram-positive diplococci with a tendency to short chain formation and in some cases to only partial retention of the methyl violet stain used. Some of these organisms were very small and in general they were smaller than the ordinary streptococcus pyogenes. No capsulated organisms were found and the examinations by Zieler's method gave the same results as that for Gram positive bacteria.

Histologically the cardiac muscle fibres were normal in appearance and showed the usual transverse striation perfectly well throughout.

The sections examined from the external wall of the *right ventricle* showed a slight general increase in the connective tissue elements and fairly well marked perivascular infiltrations, which were almost entirely lymphocytic in character with an occasional large mononuclear cell. The muscle immediately under the epicardium seemed unaffected by the proliferation of the connective tissue elements consequent on the pericarditis, a statement which holds good in the case of the ventricular wall on the left side as well as on the right.

The sections of the external wall of the *left ventricle* showed a small general increase in the connective tissue elements and small perivascular infiltrations which differed somewhat from those on the right side in that they contained a constant small proportion of polymorphonuclear leucocytes. Among the newly formed connective tissue on the surface of the ventricle a well marked giant cell lesion, in connection with a vessel and surrounded by a lymphocytic and large mononuclear infiltration, was found. Except that it occurred in obvious association with a vessel and that no leucocytes were found in the infiltration, it corresponded in all respects with the valvular lesion depicted in Fig. 5 which is fully described below.

In the *right auricle* a considerable increase in the connective tissue elements was found with extensive perivascular infiltrations of lymphocytic character. In the thickened epicardium of this region some single giant cells were seen. They had the same staining character as those described below in connection with the valves, interauricular septum and bundle, and they were in close relationship with vessels. The accompanying infiltrations were mainly lymphocytic with an occasional leucocyte.

The sections of the external wall of the *left auricle* showed perivascular infiltrations, especially marked at the surface, and a greater increase of young connective tissue than any other part of the heart examined. Giant cells were found in the thickened epicardium and several very large mononuclear cells occurred in the surrounding infiltrations which also showed leucocytes and lymphocytes.

The *auriculo-ventricular node* was deeply involved in the morbid process, particularly in the neighbourhood of the central fibrous body, where the normal appearances were completely obscured by a dense cellular infiltration of lymphocytes, leucocytes and large mononuclear cells. Throughout the remainder of the node and bundle, with the exception of the right branch, every vessel was surrounded by an infiltration composed almost entirely of lymphocytes. The infiltration in the neighbourhood of the central fibrous body contained a much larger proportion of polymorphonuclear leucocytes than any of the infiltrations in other parts of the heart, except those in the immediate neighbourhood of the giant cell lesions in the interauricular septum and the valves. The appearance of the node in the neighbourhood of the central fibrous body is shown in Fig. 7 which is a reproduction of a microphotograph taken from that region.

No giant cells or other large cells having similar staining reactions were found in any portion of the node proper. The *right branch* of the bundle was unaffected; the *left branch*, on the other hand, was surrounded by infiltrations throughout the whole of its traced course under the surface of the left ventricle. In addition to the infiltrations, which shared the general characteristics described in connection with the perivascular phenomena, the giant cell lesion which is shown in Fig. 8 was discovered in the fibrous sheath in close proximity to the fibres of this branch of the bundle. There seemed

to be some diminution in the size of the fibres at this point ; but the changes were not conspicuous and the surrounding infiltration, which was such a marked feature in the other two giant cell lesions from which illustrations are given, consisted in this region of a very few lymphocytes and polymorphonuclear leucocytes.

Fig. 6 is a drawing of a large collection of giant cells found close under the endocardium of the left auricle in the interauricular septum and well above the level of the upper portion of the node. This cell group formed a band of tissue at right angles to the internal surface of the auricle and lay close to apparently normal cardiac muscle. Its constituent cells call for no separate description, since they were similar to those of the valve lesion subsequently described. A few other groups of cells were seen having a similar arrangement and similar staining reactions but only single nuclei. These occurred well towards the left side of the interauricular septum deep in the sub-endocardial connective tissue. On the right side of the septum throughout the series there were groups of cells having from one to three nuclei ; from their staining properties they seemed to be of the same nature. Their presence was unassociated with lesions of the endothelium except at two points where local destruction had evidently taken place.

The valves showed considerable thickening, recent vegetations and numerous localised areas denuded of endothelium and covered by recent fibrinous deposits. The substance of the valves was completely vascularised ; in all segments of the mitral, aortic and tricuspid valves giant cell lesions were seen in all stages of formation. One of these valvular lesions is shown in Fig. 5 which is a drawing of a portion of the posterior aortic cusp. The giant cells in this and the other situations stained very deeply with the combination of hæmatoxylin and van Gieson used for the serial sections and their multinucleate character was difficult to establish under a low power of the microscope. The nuclei were either heaped together in the centre of the cell or evenly distributed in the protoplasm, but showed no tendency to arrangement round the cell periphery as in tubercular giant cells. The periphery of each individual nucleus stained very deeply with the hæmatoxylin and a densely staining chromatin mass of irregular size and shape was usually visible in the centre, leaving the remainder of the nucleus clear or showing only a few fine fibrils of chromatin substance so arranged as to give the appearance of a loose meshwork. The protoplasm around these nuclei had a marked affinity for alkaline dyes and stained deeply with hæmatoxylin. None of the giant cells in the heart or pericardium showed necrosis, though some stained more deeply than others ; as the latter were found among connective tissue which appeared more mature than that in which the deeply stained forms were observed, it is possible that the more faintly staining forms represented a later stage in development.

The particular lesion shown in Fig. 5 showed no connection with any vessel nor did the other similar lesions, with the exception of the examples which occurred in the thickened epicardium over the left ventricle and the right auricle. The lesions obviously associated with vessels took the stain deeply.

Large cells in groups of from four to twenty, and possessing single nuclei, were found in the neighbourhood of the multinucleate cells. They differed from the giant cells in size and numbers of nuclei only. There were many of such groups in the valves, both in the highly vascularised connective tissue and immediately underneath fibrin-capped lesions of the endocardium. In working systematically through a score of these groups all gradations from an enlarged connective tissue cell to a small giant cell with two or three nuclei seemed apparent.

On the whole these lesions correspond with those described by Aschoff and Tawara^{1, 2}, and by Carey Coombs³ in this country, as occurring in acute rheumatic infection of the heart.

My thanks are due to Dr. Thomas Lewis for the opportunity of publishing the case and for the use of the clinical notes and curves.

SUMMARY.

A case of acute infection of the whole heart, including its membranes, is described.

Partial heart block supervened eleven days before death, and continued until that event took place.

Histological examination of the heart showed the presence of a widely diffused inflammatory infiltration, conspicuous in the region of the central fibrous body and reaching its greatest intensity in the auriculo-ventricular node, where that structure lies in proximity to the central fibrous body.

The infection was a uniform one by Gram-staining organisms which were non-capsulated diplococci tending to form short chains and occurring more especially in the valves, epicardium and pericardium.

The nature of the inflammatory reaction was similar to that described by Aschoff and Tawara as being characteristic of rheumatic infection.

The lesions consisted chiefly of lymphocytic infiltrations; though polymorphonuclear leucocytes were also present in the node and around certain specialised cellular lesions.

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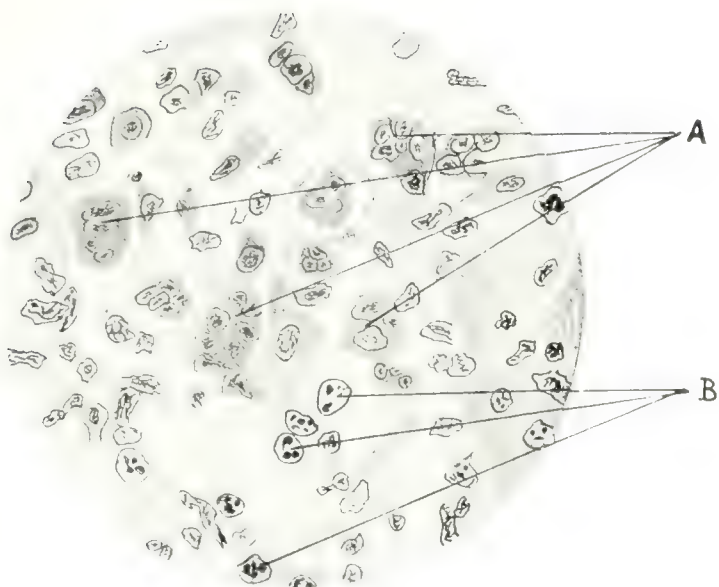


FIG. 6.

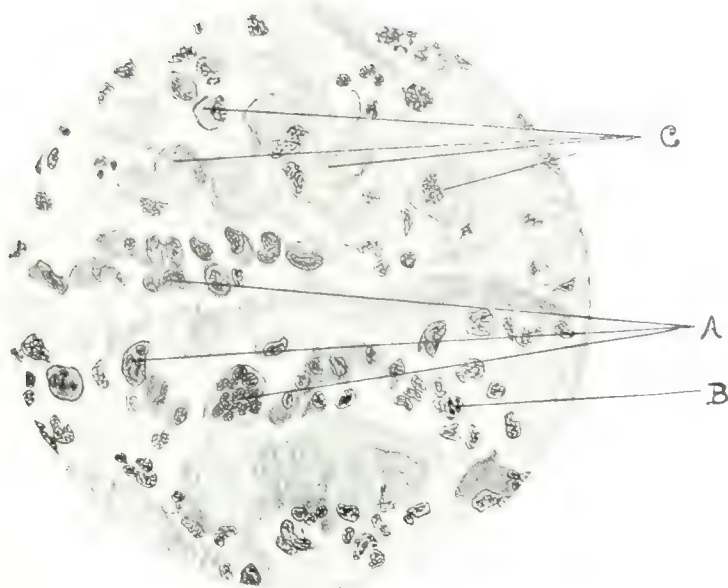


FIG. 8.

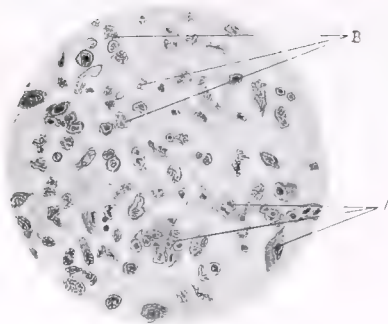


Fig. 7

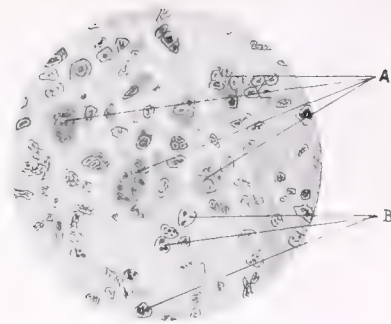


Fig. 8

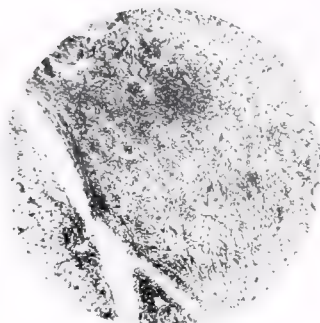


Fig. 9

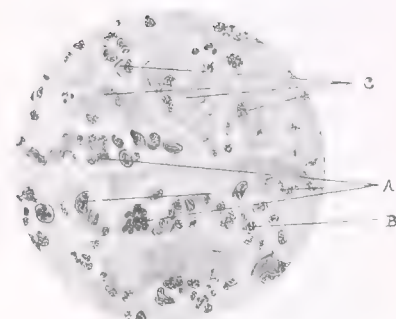


Fig. 10

FIBRILLATION OF THE VENTRICLES AT THE END OF AN ATTACK OF PAROXYSMAL TACHYCARDIA IN MAN.

BY AUGUST HOFFMANN.

(*Düsseldorf*).

A case of paroxysmal tachycardia ("heart hurry"), which, by chance, I had an opportunity of studying with the electrocardiograph at the end of an attack, seems to me to be sufficiently remarkable to permit its publication at the present time. Full knowledge of the mode of origin of the common and special crises of tachycardia, which I have designated by the use of the term "heart hurry," has not been obtained as yet. That they may be produced through nerve channels can certainly be admitted from clinical observations. In a monograph² of 1911 I put together the cases known at that time, commencing with the case recorded by Cotton in England in 1867. And I arrived at the conclusion that the tachycardial paroxysm stands by itself as a special rhythm disorder of the heart, whose cause could not receive explanation from an anatomical examination of post-mortem material. I held the view that there must be paroxysms of ventricular extrasystoles, especially because at the end of the paroxysms recorded in pulse curves, the pulse, having slowed, showed scattered ventricular extrasystoles from time to time. At a later date, and particularly as the result of observations upon a case in which at first a doubling and afterwards a quadrupling of the pulse rate was clearly and repeatedly seen in curves at the beginnings and endings of paroxysms, I was forced to adopt the view that perhaps the normal point of stimulus production might also be the seat of this special rhythm disturbance.³

In the meanwhile, it has become certain, through the electrocardiographic researches of Thomas Lewis,⁴ that the accelerated systoles of the attack, at all events so far as the ventricle is concerned, are produced through the path of the normal conducting tissues; an observation which I have also made in many cases. Hering¹ who held that it is doubtful if nerve disturbance can give rise to extrasystoles or to such paroxysms of rapid heart action as are ascribable to extrasystoles in man, for they were not found to arise so in dogs, has adopted the view, since Rothberger and Winterberg⁵ have established this phenomenon experimentally, that a combined action of vagus and accelerans may bring about a change in the position of the point of most frequent impulse formation from the Keith-Flack node to the auriculo-ventricular conducting system: the point of most frequent impulse formation controls the heart as a whole; and "nomotopic" impulses are replaced according to his view by those of "heterotopic" origin.

The electrocardiographic method gives a deeper insight into the excitatory processes associated with the heart action than any other, and analyses these processes in the human subject with the accuracy of a physiological

experiment. By means of this method, Rothberger and Winterberg⁶ have recently shown that, influenced by certain poisons, extrasystolic tachycardia may result from stimulation of the sympathetic. A determination of the events portrayed by the string galvanometer during the attack and between the attacks, and also all the happenings at the beginning and ending of the attack, must consequently have considerable interest. In the many published radial and venous curves, a notable irregularity is perceptible at the beginning and ending of the attack, before the slow rhythm passes into the fast and the reverse. The true attack of "heart hurry" begins and ends suddenly and with irregular heart beats. The irregularity at the end of the paroxysm is often introduced by a long pulse pause, which stretches over the length of several normal pulse pauses; occasionally this pause is disturbed by isolated irregular beats, and the slow rhythm, which has as a rule a rate of half that of the termination of the paroxysm, is re-established. As the apex beat and venous pulse show the same events as the arterial pulse, namely, an irregular bradycardia, so, it must be recognised that the ventricular action is slow also. This event has not been observed in the Röntgen picture, but has been inscribed by the string galvanometer.⁴

The case which I am about to describe showed special galvanometric curves at the cessation of the paroxysm.

The patient was a female cook of 26 years, who was under treatment at the time for nervous dyspepsia in my clinic. She had previously suffered from chlorosis, and had frequent discomfort of the stomach for 17 years as a result of it. The discomfort consisted of cramping pains in the stomach region and poor appetite. No blood had been vomited nor had any passed in the stools. A diffuse tenderness was present in the epigastrium, a point above the navel being especially sensitive to pressure. Examination of the stomach contents by means of a test breakfast showed well digested food material; the total acidity was 45, the free hydrochloric was 20; therefore there was no hyperacidity. Nourishing treatment produced an increase of weight of 1½ kilogrammes and abolished the discomfort in fourteen days.

On February the 28th, 1911, the patient exhibited a remarkable attack of "heart hurry," and stated that she had suffered from similar attacks from time to time, since her eighteenth year. At first they lasted $\frac{1}{4}$ or $\frac{1}{2}$ an hour, later 2 or 2½ hours. The attacks came at irregular intervals of about two or three months; and she spoke of running upstairs and emotion as the chief provocative causes. A feeling of great anxiety and weakness, but no pain, was experienced in an attack. The paroxysms began and ended suddenly.

During the attack the patient was very pale, the lungs showed no unhealthy signs, the breathing was regular, there was neither cough nor expectoration. The heart's dulness was not increased, and the Röntgen picture showed a normal heart. The heart shadow had a breadth of 12 cm.. The heart action was increased; between 180 and 208 beats per minute were counted. The heart sounds were clear and showed the phenomenon of embryocardia. At the wrist the pulse was scarcely countable, it was so rapid that the waves ran together. The blood pressure, measured after

the manner of Recklinghausen, was 140:80 cm. of water (systolic and diastolic). The apex beat was not localised; the hand, laid on the chest, felt strong and regular fluttering of the thoracic wall in the heart region.

Examination of the nervous system showed no change in sensitivity or mobility. The skin and throat reflexes were a little depressed, the tendon jerks were somewhat exaggerated. The haemoglobin content of the blood was 70 per cent. (Sahli's method). The hands trembled a little.

The attack had been brought about by shock; the patient had been told of the death of a friend in the morning. At the instant, as she received the information, the attack began. An electrocardiogram was taken, and while two leads were being simultaneously employed (lead *I*, from the right arm to left arm and lead *III*, from the left arm to left leg) using two galvanometers for the purpose, the paroxysm ceased. The pulse frequency dropped to 92. At first the pulse was irregular and small, but soon became regular. The Röntgen picture, taken immediately after the end of the attack, showed the heart to be unchanged in size. The blood pressure a quarter of an hour after the attack had risen to 160:100. The heart sounds were clear but soft.

The curves taken during the attack are of special interest. In leads *I*, *II* and *III* (Fig. 1 and 2), a great acceleration of rate is shown; the heart rate was constant throughout. The systoles have the character of typical* electrocardiograms, though in lead *I*, the variation *S* is much deeper than normal, and the curve between *S* and *T*, and between *T* and the next ill-marked *P*, is very short. *T* is well seen; *P* on the other hand is not so clear. The rate in this curve is 180 to the minute. Leads *II* and *III*, which were taken simultaneously with lead *I*, also show "typical" electrocardiograms.

The end of the attack is shown in Fig. 2 and is very special. The beats, which were regular up to this point, are now shown to be interrupted by two ventricular extrasystoles of the type described by Kraus as coming from the left ventricle. From this point they are irregular throughout; the movements of the string conform neither to "typical" nor "atypical" forms, but consist of relatively slow irregular diphasic movements, though movements having a similarity to "atypical" electrocardiograms are perceptible during this period. This irregular movement of the string continues without break for two seconds, and then two electrocardiograms of the left ventricular type follow. In leads *I* and *III* the beats run in different directions, just as they usually do when "atypical" electrocardiograms are present. This circumstance is an evidence that the swinging of the string was governed by no other movements than those of the heart, since movements of the string, such as are produced by accidental currents or voluntary movements of the patient, are in the same direction in leads *I* and *III*. Following this "delirium" of the curve, there are further regular electrocardiograms of the normal "typical" character, and they are similar in shape to those taken throughout the attack. In the curves following the paroxysm (Fig. 2 and 3), where the heart action is slow, "atypical" electrocardiograms are seen from time to

* The adjective "typische" is applied on the continent to ventricular electric curves of normal outline, as opposed to those which are termed "atypische," namely, such as are given by ventricular extrasystoles.—*Ed.*

time; and these are such as are seen as a rule in left sided ventricular extrasystoles. After some time these atypical beats are also lost from the curves.*

What do these curious events mean? An assistant, controlling the patient and feeling the carotid with the finger, remarked the end of the attack, and noted the cessation of the pulse for some while; he exclaimed "the pulse is gone." We may now explain the cessation of pulse in the radial curve in such attacks, during the recorded period of irregular bradycardia which is led up to by a long pulse pause. During the pause, large potential changes in the heart are shown. If the curves here given are compared with the irregular swings which are seen in curves of ventricular fibrillation taken from dogs, they will be found alike. In the dying hearts of dogs I have repeatedly obtained similar curves; one is shown in Fig. 6.

I believe, therefore, that at the end of the tachycardial attack, the ventricle fibrillates (as Kronecker speaks of it) for a short time, and that during this fibrillation a few weak systoles occur, until suddenly the normal rhythm is again resumed. It is very noteworthy that, ventricular extrasystoles once more disturb the normal rhythm, as shown by the "atypical" electrocardiograms, until a fully normal action of the heart is again established. This had been observed before in sphygmograph curves. The observation shows that the attacks of heart hurry consist of a severe disturbance of the movements of the heart, brought about in our patient by emotion, and manifestly through nervous channels. The end of the attack is so constituted that the controlling impulses from the normal point are removed; and this statement applies to the paroxysm also. At the transition from the fast to slow heart action a moment comes in which the ventricle responds to no regular impulses, but beats inco-ordinately, while the normal stimulus site withholds its impulses, a condition which lasts only a few seconds, until it again takes up its task as the pacemaker of the heart. It seems wonderful that the human heart should proceed apparently without observable damage after such a severe convulsion of its action, and that a termination of the phenomenon in death does not follow. But termination of the attacks in death has been observed, especially by Bouveret, and also by myself. Such a termination is perhaps explained by an absence of return of the heart from the condition, ventricular fibrillation, and the passage of this fibrillation into permanent cessation of the heart beat.

SUMMARY.

A case of paroxysmal tachycardia is described in which a paroxysm was observed, electrocardiographically, to terminate in ventricular fibrillation. The heart recovered its normal mechanism.

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- ⁵ ROTHBERGER and WINTERBURG. *Archiv f. d. ges. Physiol.*, 1910, CXXXVII and CXL.
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* The electrocardiograms during the non-paroxysmal period are similar in all three leads to those shown at the paroxysm (Fig. 4 and 5).

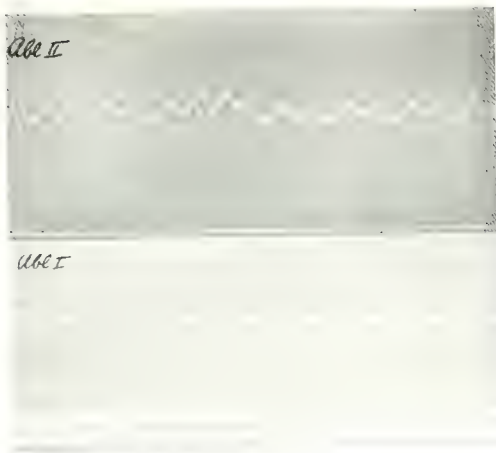


FIG. 4



FIG. 5.

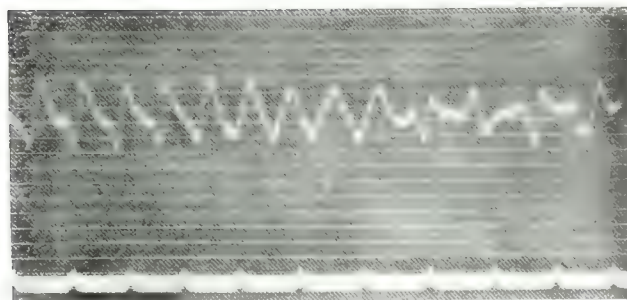
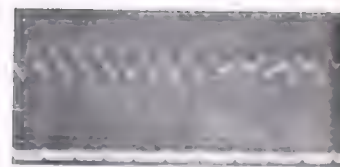
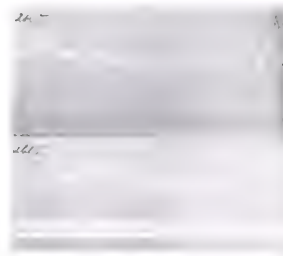


FIG. 6.



SYSTOLIC BLOOD PRESSURE.

(1) IN CHANGE OF POSTURE. (2) IN CASES OF AORTIC REGURGITATION.

BY LEONARD HILL AND R. A. ROWLANDS.

(*From the London Hospital Medical School*).

MARTIN FLACK and one of us, (L.H.),¹ by a series of observations on the systolic pressure, showed that the arm and leg readings are the same in young men, when lying quiet and in the horizontal posture. They differ by the hydrostatic pressure of the column of blood, which separates the points of measurements, when the subjects are standing or placed in inverted postures.

In these postures the pressure in the arteries of the leg varies greatly, while in the arm the pressure is kept about the same by the mechanism, which compensates for the influence of gravity.

The interesting conclusion was drawn from these observations, that the blood pressure in the ascending aorta is kept practically the same in all changes of posture. The pressure in the cerebral arteries must also be kept at approximately the same during change of posture.

We have carried out a further and more extensive series of observations on young men, and the results are given in Table I.

The Method. An armlet was placed round the upper arm, and another round the leg just below the knee. These armlets were connected to a mercurial manometer and syringe-bulb used as an air compressor, by means of suitable T pieces. The manometer employed was the single stem one used in Leonard Hill's pattern of mercurial sphygmometer. The disappearance of the pulse was taken as the index of the maximum systolic pressure, and the index was obtained from the radial artery in case of the arm, and from the posterior tibial or dorsalis pedis in the case of the leg. In the case of the last two arteries, we chose the one that gave the biggest pulse.

We made observations in the horizontal position, in the standing position and in the L-shaped position, the subject in this case lying on his back with his legs elevated. We recorded the frequency of respiration and pulse as well as the systolic pressure in each position.

Our results confirm those previously obtained. The pressure in the arteries of the arm and leg differs by the hydrostatic pressure of the column of blood, which separates the two armlets.

This column was measured in each observation by means of a metre rule and reduced in terms of millimetres of mercury. The table shows a fairly close agreement between the calculated and the recorded difference. The greatest difference between the two readings is twelve millimetres of mercury. Most of the readings agree within five millimetres of mercury. Considering the errors of observations, which arise from sensing the disappearance of the pulse, and in reading the height of the column separating one armlet from the other, the agreement seems to us to be very close.

What the nervous mechanism may be which brings about the compensation for gravity, we do not know; it is a matter for subsequent inquiry on animals.

The frequency of the pulse is accelerated in the standing posture in all the observations except three.

We have carried out a similar series of observations on old men, chosen because they had high blood pressure sclerosed arteries and no valvular disease of the heart.

In eight out of twelve of these cases lying in the horizontal position, the pressure of the brachial and tibial arteries was approximately the same, but the agreement is not quite so close as in healthy young men.

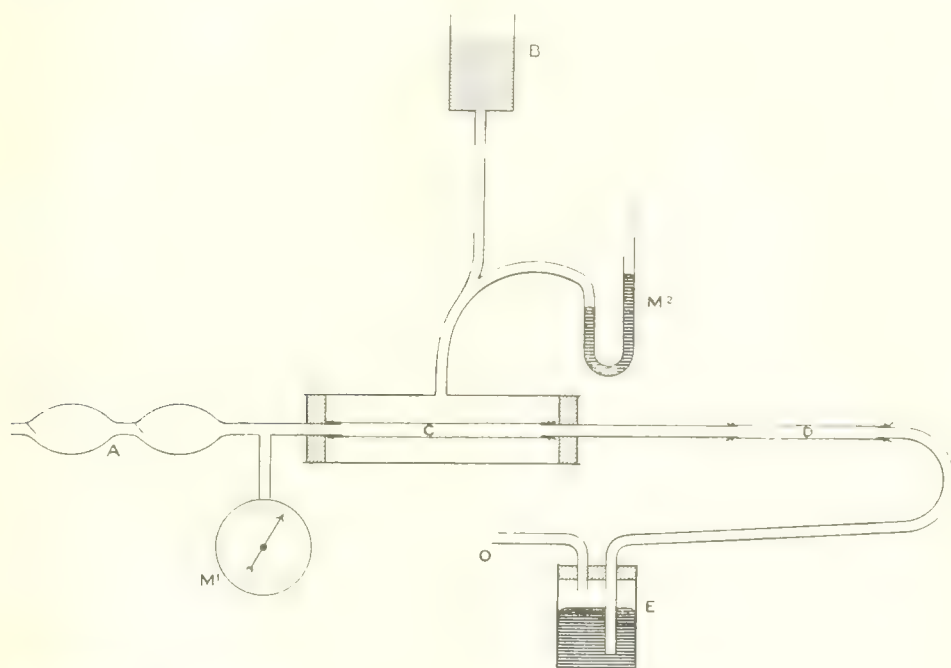
In two cases the readings differed by 10-14 mm. Hg.. In one case the difference was 34-50 mm. Hg., and in *CASE 12* no complete agreement could be found. In this case the pulse was very irregular in force and rhythm; most of the pulses could be obliterated by the same pressure in the arm and leg, but some forced their way through into the arteries of the leg, even when the pressure was raised to 300 mm. Hg.. In this case, just as occurs in cases of aortic regurgitation, the big systolic waves were much better conducted along the leg arteries than along the arm arteries. It is not a question here of rigid arterial wall, which resists compression, but one of better conductance of the crest of the systolic wave by a more contracted or stiffer artery.

Variance between the recorded and calculated differences in the three postures in three or four of these cases is very considerable, and this, we consider, is due to the varying force of the heart beat and varying conduction of the systolic wave in the arm and leg arteries. In the last part of this table the arm readings alone are recorded and both systolic and diastolic readings are given in the five last cases. In eleven out of nineteen of these cases, the pressure in the arm is lower in the standing posture, and we conclude the compensation for gravity is not so good in these.

In a paper by one of us (L.H.) written in co-operation with Martin Flack and W. Holtzmann,² results were published which show that the systolic pressures taken in the arm and leg differ widely in cases of aortic regurgitation; so much so that this difference becomes of diagnostic value. We have carried out a fresh series of observations on such cases, and the results we obtained confirm earlier ones.

In several cases we have found differences of 100 mm. Hg., and in one case a difference of 150 mm. Hg.. In the former paper it was shown that by placing the foot in warm water this difference might be diminished, and this result and other results obtained from observations on the effect of hot water baths on blood pressure of normal persons led to the conclusion that the difference was due to greater conductance of the systolic wave by the leg arteries, which are held in a more contracted state in cases of aortic regurgitation.

By means of a schema, one of us (L.H.) with Martin Flack has demonstrated that an artery made tense by a higher pressure of water conducts the crest of the pulse wave better than a soft artery containing water at a low pressure.



- A. Syringe bulb with valves.
- C. Piece of artery.
- D. Piece of artery where pulse is felt.
- E. Mercury valve for altering pressure in D.

- O. Outflow.
- M¹. Spring manometer.
- B. Head of pressure.
- M². Mercurial manometer.

The syringe bulb *A* is rhythmically worked so as to maintain a mean pressure in the spring manometer *M*¹ and the tension of the wall of *D* is altered by shifting the length of tube dipping in the mercury in *E*. The artery *C* is compressed by the head of pressure in *B*. The pulse is felt in the artery *D*. The pressure in *M*² at which the pulse disappears in *D* corresponds more closely to the systolic pressure in *M*¹ when *D* is more tense than when it is less tense.

We have found that placing the foot in hot water diminishes the difference to a certain extent.

Placing the buttocks and lower part of trunk in a bath of hot water does not diminish the difference in pressure, but if the buttocks and legs together are placed in hot water the difference is abolished. Bandaging the feet tightly did not affect this result. We believe the hot water acts by inducing vaso-dilatation of the femoral arteries and so lessening the rigidity of the wall and the conductance of the systolic waves.

It seems clear from our observations, and those of Flack, Holtzmann and Hill, that the systolic pressure, as measured in man by the sphygmometer, or by any form of spring manometer directly connected with the artery of an animal, is modified by the conductance of the arterial wall. It has been found by Hürthle and others that the systolic pressure in animals may be higher in the femoral than in the carotid artery.*

Tiglerstedt³ sought to explain this by supposing that the primary pulse wave is reflected from the periphery and adds itself to the primary without change of sign. This, we believe, is due to better conductance of the crest of the systolic wave to the femoral artery. In healthy young men, the conductance seems to be about the same, in aortic regurgitation the leg arteries are held, we believe, in a contracted state in order that the brain may receive a sufficient supply of blood.

In old age the arteries of the leg may be more rigid, and then the conductance may differ in them, and the pressures in arm and leg be unequal.

The research has been carried out with the aid of a grant from the London Hospital Research Fund.

*The following figures were kindly communicated to us by Dr. Thomas Lewis. They were taken from a dog, a month after destruction of the aortic valves, by means of a Hürthle manometer:

Brachial Artery (elbow)...	...	{ Syst.	198	...	169
		{ Diast.	74	...	89
Femoral „	{ Syst.	240	...	204
		{ Diast.	58	...	60
Posterior Tibial Artery		{ Syst.	144		
		{ Diast.	82	..	—
Brachial (high up) ..		{ Syst.	190	...	—
		{ Diast.	76	..	—

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TABLE I. SYSTOLIC PRESSURES IN MM. Hg TAKEN FROM STUDENTS AGED ABOUT 20

	SITTING POSITION						STANDING POSITION						STANDING POSITION						Remarks
	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	
B	118	118	0		2	0	118	190	71	71	90	18	117	71	53	16	70	20	
	119	119					190						70						
M	115		0	0	78	20	115	160	74.5	70.8	8	16	115	70	40	39.2	80	22	
	115						116						115	70	40	39.2			
M	121	121	0			15	121	190	67	72.5	38		126	71	53	47.7	64	16	
	121						175						71						
A.P.	130	130	0			15	132	193	62	61	38		131	73	62	47	60	14	
	137	137	0				131	193					131						
	119	119	0	0	62	18	120	190	70	72	82	20	119	74	44	39.2	60	18	
	12						120	190					119						
	122	122	2	3	64	16	122	189	64.5	64	60	16	118	70	41	39.2	60	16	
	120						187						70						
M.B.	138	138	0	0	68	12	137	203	68	69.2	8	18	140	100	78	60	90	14	
	139						138	203					138	91					
A	120	120	0	0		18	126	252	77	68.5	84	20	126	77	43.5	41	78	20	
	115						121	18					77						
S.I.	105	105	0		50	22	170	170	63.5	61	61	0	61	44.5	43.1	86	20		
	11	105					172						107	60	60	60	78	18	
S	115	115	0		74	18	110	184	70	80	80	22	117	60	60	60	78	18	
	115						110	184					117						
I.C.	123	123	0		1		120	180	60	60	80	18	117	60	4.5	60	68	26	
	125	133					121	180					117						
	125	125	0		14		120	180	78	74.00	7	14	126	78	60	60	8	16	
	128	128	0				126	180					126	78					
A	118	120	0		74	22	118	180	8	78	80	18	126	78	41	40.7	10	20	
	120	122	2	0			126	180					126	78					
C.B.	128	128	0		72	22	130	190	70	70	80	18	130	81	70	60	76	16	
	130	128	2	0			130	190					130	81					
I.C.	130	130	0		61	28	130	190	74	74	8	22	130	81	60	40	62	18	
	131	131	0	0			129	202					131	81					
	119	130	0		23	26	112	170	60	60	90	22	131	81	40	60	76	18	
	120	126	0				110	165					131	81					
	125	125	0		80	20	125	185	60	60	68	22	125	77	47.5	60	82	18	
	125	125	0		70	24	124	184	60	60	60	16	125	77	47.5	60	82	18	
	124	124	0				123	184					125	77					
	113	113	2	0	8	20	113	176	60	60	68	18	113	77	47.5	60	82	18	
	112	116	0				115	176					114	77	47.5	60	82	18	
	108	141	2	0	17	18	140	200	60	60	68	16	114	77	47.5	60	82	18	
	109	141	2	0			140	200					114	77	47.5	60	82	18	
	112	112	0		80	20	105	182	74.7	68.7	74	18	112	77	47.5	60	82	18	
	111	116	2	0			105	182					112	77	47.5	60	82	18	
M.M.	121	121	2		80	32	108	178	60	60	68	20	112	77	47.5	60	82	18	
	121	121	0				110	178					112	77	47.5	60	82	18	
	121	121	0				110	178					112	77	47.5	60	82	18	
	121	121	0				125	180					112	77	47.5	60	82	18	

Pressure in mm. Hg. taken from students aged about 20.

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TABLE II—PRESSURES IN MM. Hg. TAKEN FROM OLD MEN.

No.	Age	ARTERIAL PRESSURE					STANDING POSITION					LIE, EXTENDED—SHAPED POSITION					Diagnosis
		Systolic	Diastolic	Mean	Pulse	Rate	Systolic	Diastolic	Mean	Pulse	Rate	Systolic	Diastolic	Mean	Pulse	Rate	
1	77	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Granular kidneys
2	78	200	120	130	80	110	190	120	130	80	110	220	130	140	90	110	Arteriosclerosis and granular kidneys
3	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis
4	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis and aneurism
5	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Myocardial failure
6	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Chronic interstitial nephritis, arteriosclerosis
7	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Papae very indurated
8	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Remolitis and erythrocytosis
9	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Osteoarthritis, peripheral neuritis
10	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Hemorrhages, chronic kidney
11	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Lead poisoning, wrist drop
12	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Intermittent diabetes mellitus, arteriosclerosis
13	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis, arteriosclerosis, arteriosclerosis

* Pharyngeal catheter, placed at the lower end of the trachea, which registers only the tracheal pressure.

No.	Age	ARTERIAL PRESSURE					STANDING POSITION					LIE, EXTENDED—SHAPED POSITION					Diagnosis
		Systolic	Diastolic	Mean	Pulse	Rate	Systolic	Diastolic	Mean	Pulse	Rate	Systolic	Diastolic	Mean	Pulse	Rate	
1	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Granular kidneys
2	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis and granular kidneys
3	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis
4	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis and aneurism
5	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Myocardial failure
6	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Chronic interstitial nephritis, arteriosclerosis
7	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Papae very indurated
8	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Remolitis and erythrocytosis
9	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Osteoarthritis, peripheral neuritis
10	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Hemorrhages, chronic kidney
11	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Lead poisoning, wrist drop
12	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Intermittent diabetes mellitus, arteriosclerosis
13	78	200	120	130	80	110	200	120	130	80	110	220	130	140	90	110	Arteriosclerosis, arteriosclerosis, arteriosclerosis

TABLE III—SYSTOLIC PRESSURE IN MM. HG. TAKEN
IN CASES OF AORTIC DISEASE.

D=disappearance of pulse wave.			R=reappearance of pulse wave.				
Case.	Diagnosis.	Age.	Radial artery.	Posterior tibial artery.	Difference.	Difference of or numbers of h. 2 in lat. w. 1.	Notes.
W. G.	Aortic incompetence, mitral incompetence and stenosis.	32	<i>Left Side.</i>		70	49	P.M. examination Aortic incompetence only
			D = 100	D = 170			
			<i>Right Side.</i>				
			(Successive readings)				
			D = 106	D = 170			
			R = 106	R = 166			
			D = 105	D = 167			
			R = 103	R = 156			
			D = 104	D = 165			
			R = 103	R = 155			
H. J.	Mitral and aortic regurgitation.	17	<i>Left Side.</i>		30	10	
			D = 132	D = 162			
			<i>Right Side</i>				
			(Successive readings)				
			D = 140	D = 184			
			R = 130	R = 170			
			D = 128	D = 153			
			R = 122	R = 153			
			D = 122	D = 160			
			R = 120	R = 138			
A. S.	Aortic and mitral incompetence and arterio-sclerosis.	53	<i>Left Side.</i>		35 29	35 35	
			D = 190	D = 225			
			R = 181	R = 210			
			D = 190	D = 225			
			R = 185	R = 220			
			<i>Right Side.</i>				
			D = 190	D = 225			
			R = 190	R = 220			
			D = 180	D = 220			
			R = 184	R = 208			
D = 185	D = 225						
R = 184	R = 215						
D = 186	D = 225						
R = 185	R = 214						

Case.	Diagnosis.	Age.	Radial artery.	Posterior tibial artery.	Body temp.	Difference after immersing in hot water.	Notes.
A. S.	Mitral regurgitation and stenosis. Aortic regurgitation.	16	<i>Left Side.</i>				
			D = 110	D = 135	25		
			D = 110	D = 118		8	
			<i>Right Side.</i>				
			D = 111	D = 138	27		
			R = 108	R = 130	22		
			D = 110	D = 142	32		
			R = 98	R = 135	37		
			D = 107	D = 138	31		
			R = 98	R = 132	34		
			D = 105	D = 135	30		
			R = 100	R = 130	30		
E. B.	Aortic and mitral regurgitation. Cardiac failure.	51	<i>Left Side.</i>				
			D = 110	D = 150	40		
			D = 105	D = 140	—	35	
			<i>Right Side.</i>				
			D = 110	D = 150	40	—	
			R = 104	R = 145	41	—	
			D = 110	D = 150	40	—	
			R = 104	R = 145	41	—	
			D = 110	D = 155	45	—	
			R = 103	R = 145	42	—	
			D = 111	D = 150	39	—	
			R = 105	R = 140	35	—	
C. F.	Mitral and aortic regurgitation.	19	<i>Left Side.</i>				
			D = 120	D = 165	45		
			R = 115	R = 165	50		
			D = 115	D = 140	—	25	
			R = 110	R = 138	—	28	
			<i>Right Side.</i>				
			D = 120	D = 160	40	—	
			R = 112	R = 150	38	—	
			D = 125	D = 160	35	—	
			R = 112	R = 150	28	—	
			D = 125	D = 160	35	—	
			R = 115	R = 150	35	—	
G. M.	Aneurysm of aortic arch.	41	<i>Right Side.</i>				
			D = 103	D = 150	47	—	
			R = 95	R = 148	53	—	
			D = 104	D = 150	46	—	
			R = 90	R = 135	45	—	
			D = 103	D = 140	—	37	
			R = 100	R = 135	—	35	

Case	Diagnosis	Age	Position of limbs	Position of limbs	Diastolic	Diastolic and pulse rate in 100 beats	Notes
G. M. (cont.)			<i>Left Side.</i>				
			D = 140	D = 150	10		
			R = 140	R = 150	10		
			D = 140	D = 150	10		
			R = 140	R = 150	10		
			D = 140	D = 150	10		
			R = 140	R = 150	10		
E. H.	Aortic regurgitation	25	<i>Left Side.</i>				
			D = 135	D = 160	25		
			D = 130	D = 155	25		
			D = 130	D = 152	22		
			D = 125	D = 152	27		
			D = 125	D = 150			
			<i>Right Side.</i>				
			D = 132	D = 160	28		
			D = 131	D = 140		9	
H. J.	Aortic regurgitation.	42	<i>Left Side.</i>				
			D = 140	D = 190	50		
			D = 138	D = 190	52		
			D = 135	D = 182			
			D = 132	D = 182	50		
			<i>Right Side.</i>				
			D = 140	D = 190	50		
			D = 140	D = 195	55		
			D = 140	D = 165		25	
N. G.	Aortic regurgitation and stenosis.	35	<i>Left Side.</i>				
			D = 140	D = 226	86		
			D = 140	D = 225	85		
			D = 135	D = 242	107		
			D.P.A.				
			D = 135	D = 244	109		
			D.P.A.				
			D = 135	D = 239	104		
			D.P.A.				
			D = 135	D = 199	64		
			D = 135	D = 185	60		
			D = 134	D = 185	51		
			<i>Right Side.</i>				
			D = 130	D = 246	116		
			D.P.A.				
			D = 130	D = 224		94	
			D.P.A.				
			D = 130	D = 225		95	
			D.P.A.				

D.P.A. means Dorsalis Pedis Artery.

Case.	Diagnosis	Age.	Radial artery.	Posterior tibia. artery.	Difference.	Difference after immersing in hot water.	Notes
W. M.	Aortic regurgitation	37	<i>Right Side.</i>				
			D = 145	D = 220	75		
			D = 145	D = 210	65		
			D = 143	D = 210	67		
			D = 140	D = 210	70		
			D = 150	D = 230	80		
			(D.P.A.)				
			D = 145	D = 230	85		
			(D.P.A.)				
			D = 140	D = 225	85		
			(D.P.A.)				
			<i>Left Side.</i>				
			D = 140	D = 220	80		
			D = 140	D = 230	90		
H. B.	Aortic regurgitation	47	<i>Right Side.</i>				
			D = 153	D = 255	102		
			D = 158	D = 258	100		
			D = 155	D = 255	100		
			D = 156	D = 256	100		
			D = 153	D = 290	137		
			(D.P.A.)				
			D = 158	D = 291	133		
			(D.P.A.)				
			D = 155	D = 280	125		
			(D.P.A.)				
			D = 156	D = 284	128		
			(D.P.A.)				
			<i>Left Side.</i>				
T. N.	Aortic and mitral regurgitation.	55	D = 140	D = 290	150		
			(D.P.A.)				
			D = 142	D = 295	153		
			(D.P.A.)				
			D = 144	D = 295	151		
			(D.P.A.)				
			D = 143	D = 293	150		
			(D.P.A.)				
			D = 140	D = 276		136	
			(D.P.A.)				
			<i>Right Side.</i>				
			D = 145	D = 185	40		
			D = 140	D = 185	40		
			D = 137	D = 180	43		
			D = 137	D = 179	42		
			D = 145	D = 170	25		
			(D.P.A.)				
			D = 145	D = 175	30		
			(D.P.A.)				
			D = 137	D = 170	33		
			(D.P.A.)				
			D = 137	D = 169	32		
			(D.P.A.)				
			<i>Left Side.</i>				
			D = 145	D = 185	40		
			D = 145	D = 170		25	

HORIZONTAL POSTURE.

M. F.
I.

Right brachial artery.

110
110
102

Right posterior tibial artery.

152
155
159

II. The right foot was then placed in hot water and records again taken.

102
105
105
109

161
161
165
175

III. Lower part of body trunk placed in hot water, legs out, and record again taken.

Left brachial artery.

113
113

Left posterior tibial artery.

159
155

IV. Both legs and buttocks placed in hot water.

112
102
102
102

125
110
125
115

V. Left foot and right foot and leg bandaged tightly.

101
102

108
112

AORTIC REGURGITATION.

HORIZONTAL POSTURE.

L. S. Age 16.

I.

Left brachial artery.

110
112

Left descending aorta.

170
165

II. Buttocks and lower part of trunk placed in hot water.

110
110
109

170
168
170

III. Both legs and buttocks placed in hot water.

110
105

110
105

HORIZONTAL POSTURE

E. S. Age 37.

I.	<i>Left brachial artery.</i>		<i>Left posterior tibial artery.</i>
	130		240
	135		240
	130		245

II. Buttocks and lower part of trunk placed in hot water.

	127		195
	130		210
	130		220

III. Buttocks and legs placed in hot water.

	130		140
	135		145
	135		135
	130		130
	128		130

N.B. — Rectal temperature immediately after last immersion, = 101.2 degrees F. d r.

AURICULAR FIBRILLATION AND HEART-BLOCK IN DIPHTHERIA.

BY FREDERICK W. PRICE.

(*London*).

AND

IVY MACKENZIE.

(*Glasgow*).

WHAT has often been termed "cardiac paralysis" in diphtheria has long been recognised to be associated in the majority of cases with extensive myocarditis. More recent investigations on the subject tend to suggest that the marked slowing of the pulse in many of these cases is due to a condition of dissociated auriculo-ventricular rhythm, and there are at least two cases in the literature (Fleming and Kennedy¹ and Magnus-Alsleben²) in which clinical heart-block was demonstrated and in which post-mortem examination revealed a degenerative condition of the auriculo-ventricular bundle. In these cases, there was, in addition to the disease in the bundle, a widespread degeneration and cellular infiltration of the auricular and ventricular muscle. The following case of cardiac failure in diphtheria was characterised by the sudden incidence of an abnormally slow and regular radial pulse. The polygraph tracings suggest that the slow ventricular rhythm was not accompanied by an independent auricular rhythm, but that the auricle was in a state of fibrillation. This is the first recorded instance, so far as we know, of a case of this kind occurring in diphtheria, although a similar clinical phenomenon has been noted by Mackenzie in other cardiac affections. (*"Nodal Bradycardia," Heart, 1910, I, Cases 2 and 4.*)

M. H., female, aged 9, was admitted to the South Western Fever Hospital, Stockwell on October the 28th, 1910, with the following history—

On October the 26th she was quite well. On the 27th she suffered from headache, vomiting, and sore throat. On the 28th the glands of the neck were noticed to be enlarged. There was a previous history of measles and whooping cough.

On admission to hospital, the patient's face was flushed, and circumoral pallor was well marked. There was a faint erythema, not definitely punctate, on the arms. The tongue was covered with a white fur, the papillæ showing up and the tip seemed peeling. There were no Koplick's spots. The tonsils were greatly swollen and met in the middle line; they showed slight exudate and a good deal of superficial ulceration. The glands of both sides of the neck were enlarged. There were no discharges. The temperature was 102 degrees Fahr. . Antitoxin (12,000 units) was injected.

Course. On October the 29th the patient had rather a restless night. She was taking her food well. There was no rash. Nasal distension was present. The tongue was thickly coated, and there was some faucial swelling and œdema, with a thin pearly exudation on the tonsils, soft palate and front part of the hard palate. Glandular swelling and œdema of the left side of the neck were present. The temperature came down to 98·4°; in the evening it was 99°. At 6 p.m. the patient was restless, and vomited twice slightly. At 11 p.m. she vomited after alcohol had been given. Antitoxin (12,000 units) was administered.

On October the 30th, the tongue was dirty, the membrane extended over the soft palate and on to the hard. The temperature varied from 97.2° to 99°. The pulse was 96 in rate and regular and the tension seemed raised. Antitoxin (12,000 units) was injected.

On October the 31st the patient took her food better and there was no vomiting. The faucial swelling had disappeared, and there was a whitish exudate, more on the left side of the soft palate and separating. The glands were palpable. The pulse was 84 and regular. The apex beat was inside the nipple line. The heart's sounds were rather weak.

On November the 1st the patient took her food fairly well and there was no vomiting. The exudate was discoloured and separating. She was passing a fair amount of urine, in which there was a trace of albumin. The temperature ranged from 97.2° to 98°. The pulse was 44 per minute and soft. The apex beat was in the nipple line. The first sound was muffled and the second sound thumping in comparison.

On November the 2nd a fair amount of urine was passed, in which there was a trace of albumin. The exudate on the throat was very much less. The extremities were cold, and the temperature was 97° (it remained at this level). The pulse was 40, and the second sound at the base was reduplicated. At 5 p.m. and at 7 p.m. the patient vomited.

On November the 3rd. In the twenty-four hours 30 oz. of urine were passed, in which there was no albumin. The pulse was 34, and the tension appeared to be lower. The surface of the body was very cold. The pulse was 48. The hepatic dulness in the nipple line was much the same as before, but in the epigastrium it was more evident.

On November the 4th the patient took her food well. She vomited three times during the day: 33 oz. of urine were passed, in which there was a small quantity of albumin. She was cyanosed. The pulse was 40 per minute, regular, small, and the tension appeared lower. The apex beat was well outside the nipple line, the impulse being so feeble as to be only just perceptible. The sounds were faint, and the second, at the base, was reduplicated.

On November the 6th the patient died.

During the course of the illness the patient was treated by local applications to the throat, brandy, hot port wine, hypodermic injections of atropine, strychnine and adrenalin, etc..

Marked slowing of the pulse is, as we have noted, a phenomenon not infrequent in severe and particularly in fatal cases of diphtheria. In this case the pulse fell from a rate of 84 to 44 beats per minute within the space of a few hours on about the sixth day of the disease. The problem, however, is whether we have to deal with a condition of partial or complete heart-block. This is not easy to determine. At first the writers were inclined to the view that the case was one of partial heart block with a 2 : 1 rhythm. For while the principal waves throughout the tracing occur in the period 3-6, here and there, and sometimes for two or three beats in succession, a wave marked *o* is seen in the period 1-3, which, when taken by itself, is sufficiently definite to suggest a normal contraction of the auricle. Further, there is a pronounced wave marked * which recurs constantly and immediately after the fall *y*. This wave falls regularly with the preceding and following waves marked *o*, when these are present.

But the wave *o* seen in the period 1-3 is not constant over long stretches of tracing. On the other hand there are fine oscillations in the diastolic phase, which, although ill-defined, are probably the result of fibrillary movements of the auricle, and this explanation would serve for the waves in the period 1-3.

The only constant and prominent waves other than those marked * fall within the sphygmie period, suggesting the ventricular form of venous pulse.

It has been demonstrated by experiment and confirmed by clinical observation that in completely dissociated auriculo-ventricular rhythm, the ventricular beat is regular in force and rhythm and is slower than normal. In the case under consideration the presumption is that we are dealing with

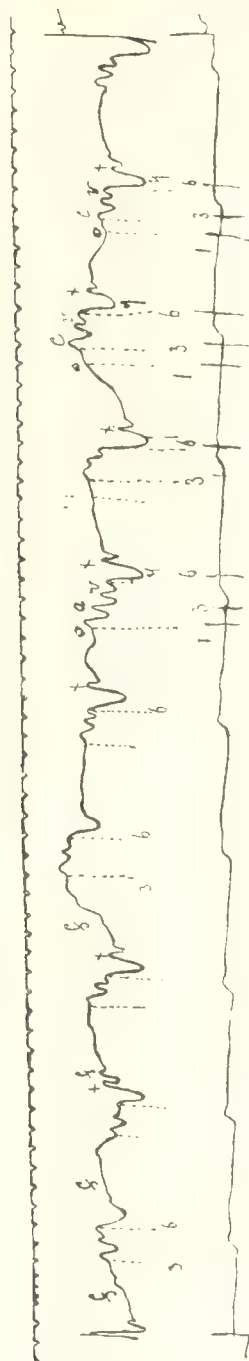


FIG. 1

an independent ventricular rhythm in a heart where the auricles were in a state of fibrillation.

Assuming that a condition of auriculo-ventricular block with fibrillation of the auricles is present, it remains to explain the early diastolic wave. This is believed to be the wave described by Hirschfelder and Gibson, and called *h* or *b*.

Post-mortem Examination of the Heart.

The heart was soft and flabby and appeared to have been in diastole when vital movement ceased. The ventricular chambers were greatly distended. There was no evidence to the naked eye of hypertrophy of the muscle. The tricuspid and mitral orifices appeared to be wider than is usual in a heart of this size. The right auricular appendix was filled with a thrombotic mass. The heart was fixed and preserved in methylated spirit; it was impossible to be certain as to its content in fat. Sections were frozen and cut and subsequently stained with Sudan *III* solution, but no evidence of fatty degeneration of the muscle fibres could be found. The tricuspid, mitral, pulmonary and aortic valves presented normal appearances. The coronary arteries appeared to be normal.

For further histological examination the following pieces of the organ were excised (1) a small portion at the junction of the superior vena cava with the right auricle; this included the sulcus terminalis, the adjoining portion of the right auricle and right auricular appendix, a small portion of the tinea terminalis and about three-fourths of the circumference of the origin of the superior vena cava. (2) A block of tissue including the auriculo-ventricular node and bundle, with the commencement of the right and left divisions of the main bundle. This block extended backwards to the opening of the coronary sinus and forwards to a point about 1 cm. in front of the pars membranacea septi. It had on one side the points of attachment of the septal cusp of the tricuspid valve and on the other the aortic cusp of the mitral valve and a portion of one of the aortic cusps of the aorta. The block included a small portion of the intraventricular septum, about 1 cm. below the auriculo-ventricular groove, and the upper border was cut parallel to the groove on the right side and about 2.5 cm. above it. (3) A small portion of the posterior wall of the auricles between the superior vena cava and the entrance of the right pulmonary veins was excised. This block contained the large ganglia and nerve trunks which correspond probably to Remak's ganglia in the frog. (4) Fourteen other blocks were taken from various parts of the heart, including auricles, moderator band, papillary muscles and ventricular walls.

In the first place, the block which included the sino-auricular node was cut in a series of sections in a plane at right angles to the lumen of the superior vena cava. Every fifth section of the series was mounted and stained with hæmalum and Van Gieson's solution. Examination of the sino-auricular node failed to reveal any histological appearance which would be regarded

as abnormal. There was a very considerable amount of fibrous tissue in the region of the node, but this is a condition which has been noted in hearts which clinically present no abnormality. The amount of tissue in normal sino-auricular and auriculo-ventricular nodes has been recognised to vary very much within normal limits. The main point in regard to this series is that neither in the node itself nor in the muscle tissue in immediate association with it was there any evidence of degeneration or infiltration. A considerable number of nerve trunks and ganglionic masses appeared in the sections, but nothing abnormal was detected in them.

In the second place, the block including the auriculo-ventricular node and bundle was cut in series. The sections were cut at right angles to the course of the bundle, that is, in a plane parallel to the anterior aspect of the heart. This is not the method most frequently employed, but we have found it most convenient as regards orientation in smaller hearts, and have regularly pursued it in the examination of large hearts also. The sections were mounted in series, every fifth section being taken from the posterior half of the block, and every tenth of the anterior half. The sections were stained with hæmalum and Van Giesen's stain. The sections were examined from the auricular connections of the node to the disappearance of its two main subdivisions into the right and left ventricles respectively. In no part of its course was there any evidence of acute degeneration of the muscle fibres or of infiltration of cells. The muscle fibres in some parts presented a vacuolated appearance, which is characteristic of the normal node and bundle fibres in ungulate hearts, but the nuclei seemed normal and took the stain in a normal fashion. The vessels appeared to be normal also. In striking contrast with the tissue comprising the node and bundle was the muscle of the intraventricular septum in its immediate neighbourhood. Here the septal spaces between the muscle bundles were invaded by small round cells which were, for the most part, of the formative type. The muscle fibres themselves were swollen from place to place in the sections. The nuclei varied greatly in size, but stained normally. The tissue of the interauricular septum in the sections belonging to this block did not show these appearances of degeneration and infiltration.

In the third place a series of section was made from the posterior wall of the auricle which included the large nerve trunks and ganglionic masses in this region. Nothing abnormal however was detected.

In the fourth place the blocks from various other parts of the auricle and ventricle were examined, and in these were found varying degrees of degeneration and infiltration. On the whole the degeneration and infiltration in the auricles was slight compared with that in the ventricles. For example, thirty sections from the tinea terminalis were examined and no evidence of degeneration was seen. These sections were cut in a plane parallel to the course of the fibres. On the other hand in some parts of the sections from the ventricles the degeneration and infiltration were very advanced (Fig. 2). The cardiac tissue seemed to be partly digested by the

inflammatory exudate. Only small fragments of muscle fibres were seen in some fields. The exudate was composed largely of cells of the formative type with round or oval nuclei. Occasionally, however, polymorphs were present. In those parts in which the destruction was less advanced, the exudate could be seen to be primarily around small vessels and the presence of abnormally large nuclei in some of the muscle cells could easily be made out (Fig. 3).

Although the muscle fibres were swollen and broken up in some parts, there was no evidence of breaking up or of the feeble staining of the muscle nuclei, which is associated with cloudy swelling. The degree of degeneration varied greatly in different parts of the heart and was perhaps most marked in the sections of papillary muscles and trabeculae, but there was evidence of degeneration in every section examined from the ventricles, although in some sections the evidence of disease was slight and confined to perhaps one small area.

Summary of Histological Examination.

The heart showed extreme degeneration and cellular infiltration of cardiac muscle, especially in the ventricles, occurring in scattered foci of unequal size and distributed largely in the course of the vessels. These changes did not involve the sino-auricular node or bundle. There was no evidence of change in the nerve trunks and ganglionic masses which were examined in the posterior walls of the auricles. Whether the vacuolated appearance of the fibres in the auriculo-ventricular node could be taken as evidence of degeneration of a fatty character, it would be impossible to say, but the appearance did not differ from that seen in normal hearts of lower mammals, although it is not common in the human heart.

COMMENTS.

The fact that experimental heart-block can be produced in animals by destruction of the auriculo-ventricular node and bundle has given an impetus to the anatomical and histological study of these structures in the human subject. In a fairly large percentage of cases of heart-block in man, lesions of a gummatous or sclerotic character have been described in the node or in the main bundle. While the bundle has been completely destroyed in some cases, in others the condition described is that of "considerable sclerosis," or "a tendency to sclerosis," or "the bundle in half its extent invaded by connective tissue," or "fatty infiltration and degeneration of the bundle." On the other hand two cases have been described in which there was clinical evidence of heart-block and post-mortem examination showed the node and main stem of the auriculo-ventricular special muscle to be devoid of any particular lesion. In Fahr's case³ he could find no gross

Longitudinal
the muscle
signification

Higher in
small round
date rough
disintegration

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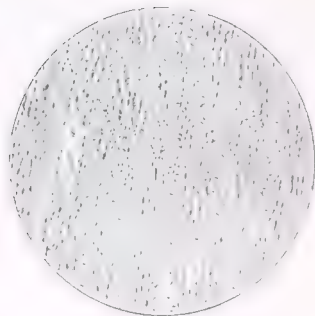


FIG. 2

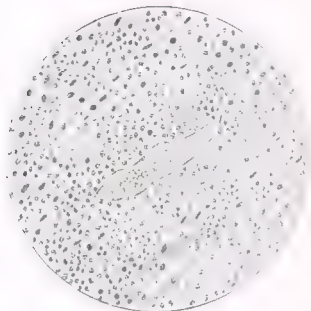


FIG. 1

or microscopic lesion, although he admits that the bundle was not examined in all its ramifications. In Krumbhaar's case⁵ there was a diffuse fibrotic change in the ventricular muscle, but no lesion of the node or bundle. Krumbhaar suggests the possibility of heart-block being in some way associated with an excessive fibrosis of the sino-auricular node. This, however, is an explanation which must be accepted with reserve, because the relation of the sino-auricular node to auriculo-ventricular dissociation is a matter on which we possess no data, and a fibrotic condition in the region of the node is a common occurrence in hearts which present no clinical abnormality.

Again, cases of heart-block have been described by Earnshaw² and Taylor⁸ where the heart-block passed off, leaving a normally contracting heart, so far as the tracings could show. Lewis and Mathison⁶ have shown that heart-block may be produced by asphyxia, and Florence Buchanan¹ has pointed out that heart-block occurs physiologically in hibernating animals.

Thus there is ample evidence to show that heart-block is not necessarily due to recognisable tissue change in the node or bundle at the auriculo-ventricular junction.

It might reasonably be contended that in a case of diphtheria the acute toxic affection produces functional disorders of the auriculo-ventricular bundle without manifesting corresponding anatomical changes. But such an explanation is unsatisfactory, in view of the extensive degeneration of the ordinary cardiac muscle which is itself an evidence of toxic influence. Whatever influence the bundle may exercise in the production of co-ordinate movements, it is absolutely necessary that the muscle tissue itself should be capable of responding normally. An abnormal bundle between a normal auricle and normal ventricle produces dissociation. It is not improbable that in this case dissociation is due to abnormalities in the tissue of the auricles and ventricles themselves. A normal node and bundle would be insufficient to produce co-ordinate contraction if the auricular and ventricular disease were such as to render ordinary auricular and ventricular contraction impossible. It is not impossible that in this case the perivascular disturbance of the lesions possesses some significance. Whatever be the function of the nerves which accompany the small vessels in the cardiac musculature, they cannot but have been affected in the process. They are lying in parts in those areas where the toxic influences have been most active. Whether their formation is associated with vasomotor influence or blood supply or nutrition, they must undoubtedly have been influenced by the acute toxic process in this neighbourhood.

No definite anatomical lesions have been found to be characteristic for auricular fibrillation. The phenomenon is often present in hearts whose auricular muscle is degenerate, but in other cases the auricular muscle shows no changes which could be regarded as responsible for the condition. In the present case there was evidence of degeneration of the auricular muscle and

in addition the dilatation of the whole heart and the advanced disease of the ventricles was incompatible with the proper nutrition of the cardiac musculature.

We wish to thank Dr. Ford Caiger, of the South-Western Fever Hospital, London, for permission to publish this case.

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THE AURICULAR FORM OF LIVER PULSATION AND ITS RELATION TO TRICUSPID STENOSIS.

BY H. HUME TURNBULL AND H. T. WIEL.

(*From Dr. Mackenzie's clinic at Mount Vernon Hospital, London.*)

MACKENZIE (*The Study of the Pulse*, 1902, page 196) has stated that the force required to produce a liver pulsation is greater than that required to produce a pulsation in the veins, and has expressed the view that auricular pulsation of the liver is rare because the normal right auricle develops insufficient pressure waves to produce it. As tricuspid stenosis is a cause of hypertrophy of the right auricle, he pointed out that a liver pulse of the auricular type would be suggestive of tricuspid stenosis. This view was strengthened by the post-mortem examination of seven cases of tricuspid stenosis in each of which a liver pulse of the auricular form had been present during life. The auricular form of liver pulse was consequently regarded by him as a possible sign of tricuspid stenosis. The case now recorded showed a well marked auricular liver pulse during life while the autopsy revealed no stenosis of the tricuspid orifice.

The patient was a boy of 18 years of age who had suffered from a series of attacks of rheumatic fever five years before he was admitted to the Mount Vernon Hospital under the care of Dr. Mackenzie in March, 1910. Although of poor general physique he had been working for some months as a blacksmith's apprentice, and was compelled to use a 7lb. hammer which left him exhausted each night. The immediate cause of his admission was the onset of palpitation and breathlessness, which had troubled him for five weeks. These attacks occurred from ten to fifteen times a day and each lasted about ten minutes. He had to sit down during the attack; at other times he could get about the house, but felt weak. There was never any dropsy.

On examination, the heart's dulness extended from $1\frac{3}{4}$ inches to the right of the mid-line to $4\frac{1}{4}$ inches to the left, the apex beat being forcible and visible in the sixth intercostal space.

A loud systolic and a diastolic murmur was heard in all areas, the systolic being louder at the apex, the diastolic at the second right costal cartilage. The pulse was regular, 88 to the minute, and the vessel wall thickened. Capillary pulsation was conspicuous and the systolic blood pressure was 98 mm. Hg.. The liver was large and pulsated; a conspicuous auricular wave was present both in the jugular and liver tracings.

For two days after his admission he remained fairly well, though the temperature rose daily to about 100°, without any obvious cause. On the third day he had an attack of paroxysmal tachycardia. While resting quietly in bed, the patient suddenly said he felt a fluttering of his heart. His face assumed an extremely anxious expression, the cyanosis increased markedly and moist râles were audible at the bases of the lungs. The pulse and heart became irregular. These conditions persisted for about ten minutes, the suffering being excessive, when suddenly the patient gave a long deep sigh, the face assumed an expression of relief, and he announced that the attack had passed off.

These attacks continued at the rate of one or two daily for about six days, and then ceased. The last gave rise to more acute distress than any of the others, the cough being severe; it was accompanied by pain over the left ribs. During this attack, the heart was noted to be beating slowly and regularly.

During the paroxysms of tachycardia the heart sometimes beat regularly, sometimes irregularly. From the jugular curves the exact mechanism was not certain, but the attacks probably consisted of paroxysms of regular tachycardia of auricular origin or auricular fibrillation. Between the attacks premature contractions arising in the auricle interrupted the regular and slow rhythm.

The curves which show the auricular form of liver pulse are illustrated by Fig. 1, 2 and 4; a curve from the abdominal aorta (Fig. 3) is also given for comparison.

The tracing obtained from the liver, which was very large and pulsated markedly, was always of the auricular type, *i.e.*, the large wave was pre-systolic in time and therefore due to auricular systole throwing a large volume of blood into the liver, the wave of ventricular systole (*v* in Fig. 4) being small and insignificant by comparison. The liver tracing shows the extrasystoles very clearly as smaller premature waves, also occurring before the time for the beginning of ventricular systole.

In tracings of the liver pulse taken near the mid-line of the abdomen (Fig. 1) a wave is seen towards the end of the large wave and giving the latter greater width.

In tracings taken farther to the right of the abdomen (Fig. 2) this wave is much less prominent, only a slight break in the fall of the *a* wave being seen, so that it was thought probable that the wave was not really a portion of the liver pulse itself, but was transmitted from some neighbouring pulsating structure, and most probably from the aorta. On comparing a tracing of the abdominal aorta taken just below the liver (Fig. 3) it is found that the time from the commencement of its upstroke to that of commencement of the radial pulse is the same as that between the beginning of the wave under discussion in the liver tracing and the radial pulse. Thus it seems probable that this wave was merely transmitted from the abdominal aorta and was not a real early systolic wave in the liver pulse.

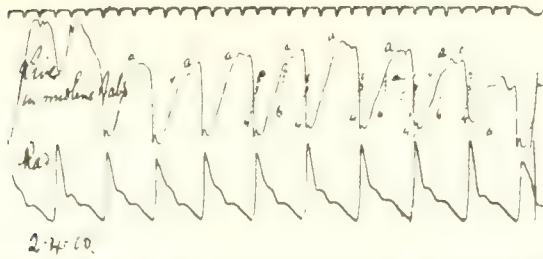


Fig. 1. A tracing of the liver pulse taken in the mid line of the abdomen. It shows a broad peak, the latter part appearing as a distinct wave. The time of the radial pulse is marked on the liver tracing at 4. 6 marks the time of opening of the tricuspid valves.

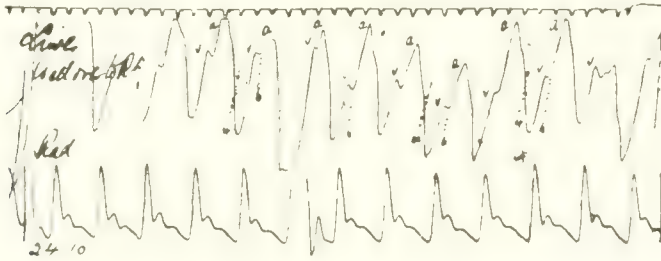


Fig. 2. Shows a liver tracing taken well over to the right. The peak of the main wave is much narrower and there is only the merest trace of a notch on the downstroke.

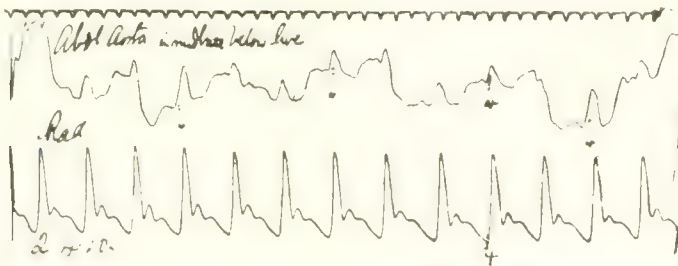


Fig. 3. A tracing of the abdominal aorta below the liver, just about the umbilicus. It shows the relation of the aortic pulse to the radial. 4 marks the time of the radial pulse.

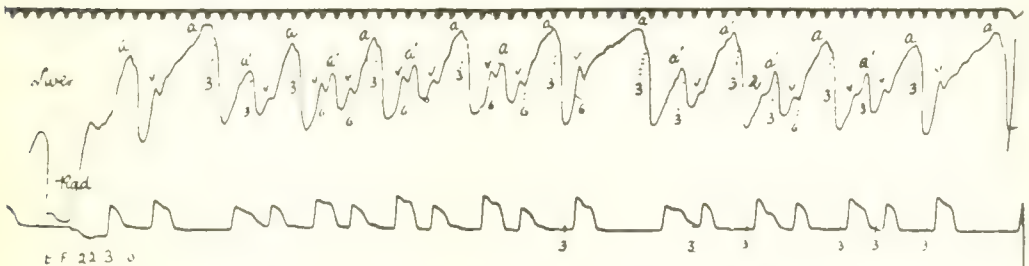


Fig. 4. Shows auricular extrasystoles in the liver pulse, the large first rise of the wave in the liver being due to a back flow of blood from auricular systole, both in the large beats and the extrasystoles.

The patient was seized with a febrile attack from an unrecognised cause and died after several months' stay in hospital. The heart was sent to Professor Woodhead and the following is an abstract of his report :—

Pathological report.

The pericardium showed old adhesions over the outer side of upper half of the left auricle and also over the aorta and pulmonary artery. The heart weight was $26\frac{1}{2}$ ozs. ; without the pericardium it weighed 19 ozs.. The length of the cavity of the left ventricle was 8.5 cm., the wall having a thickness of from 1.5 cm. to 0.5 cm.. Some thickening of the apices of the *musculi papillares* was present. The mitral valves were adherent at their free margins. Small vegetations were seen at the lower portion of the somewhat funnel shaped orifice ; the cusps were contracted. The aortic orifice was somewhat narrowed, the cusps were thickened and slightly contracted ; there were small granular vegetations along their thickened margins ; the aorta showed no atheroma. The *chordæ tendineæ* were opaque and slightly contracted. The coronary arteries were slightly thickened and narrowed. The cavity of the right ventricle was 6 cm. in length, the muscle was mottled. The pulmonary and tricuspid cusps were normal. The right auricle was dilated, the coronary vein very wide, and there was some thickening of the endocardium, especially at the base of the tricuspid valves.

CONCLUSIONS.

The auricular form of liver pulse is not necessarily associated with stenosis of the tricuspid orifice.

OBSERVATIONS ON A CASE OF HEART-BLOCK ASSOCIATED WITH INTERMITTENT ATTACKS OF AURICULAR FIBRILLATION.

BY A. W. FALCONER AND GEORGE DEAN.

(*Aberdeen.*)

J. J., male, aged 45, was admitted into the Aberdeen Royal Infirmary on July the 13th, 1911, under Dr. Edmond, to whom we are indebted for permission to observe the case.

Past history and habits. About 23 years before admission to hospital the patient had suffered from some form of venereal disease. He apparently had gonorrhœa, but no history of a definite chancre or of secondary symptoms could be obtained. Apart from this he had always been healthy and able for his work as an ironworker. He was married and had a family of six, all of whom were said to be healthy. He was a moderate drinker of spirits and smoked about three ounces of tobacco a week.

Present affection. For some years he had been troubled off and on with breathlessness on exertion. This would trouble him for a few days or a few weeks, but it always disappeared without any special treatment. On being questioned he stated that for some months previous to admission he had occasionally suffered from giddy attacks lasting a few seconds. During these attacks his sight became dim and his head "went round." He had never fallen or become unconscious. A fortnight before admission his breathlessness became much worse and was produced by the slightest exertion. The breathlessness increased until he was unable to lie flat in bed with comfort; his feet began to swell.

On admission the patient was found to be a well developed man. There was slight orthopnoea. There was very slight pitting on pressure over the ankles. The apex beat of the heart was situated in the 5th space $\frac{1}{2}$ inch outside the nipple line. At the apex the 1st sound was loud and booming, the 2nd sound was followed by an early diastolic murmur. Over the aortic area there was a well marked double murmur. The peripheral vessels were distinctly degenerated. The liver dulness extended 1 inch below the costal margin, but the lower edge could not be felt. The urine averaged about 40 ounces a day and did not contain albumen. The lungs, apart from slight emphysema, appeared normal. During his stay in hospital the patient gradually improved and soon became perfectly comfortable while in bed. In the beginning of September he was allowed up, and was able to walk about

the ward without discomfort. He left the hospital on September the 20th, 1911, but was readmitted on October the 24th. He stated that for the first few days after going home he felt fairly well, but one day he suddenly fainted, and since that time he had not been so well. His breathing had gradually got worse, and he had to return to bed. On readmission his general appearance was much worse than on his first admission. There was considerable dyspnoea and distinct cyanosis. The physical signs in the heart were the same as on the previous admission, except that the pulse rate was much slower and the individual beats much weaker. On October the 26th the pulse rate fell to 20 and the patient died that night without so far as was known any alteration in the pulse.

The polygraphic tracings.

For the first few days polygraphic tracings were taken daily. From July the 13th to the 19th the rate of the pulse varied from 48 to 42 a minute. It was invariably quite regular and, although many yards of tracing were taken, there was never any sign of a normal *a* wave either in the phlebogram or the cardiogram. Fig. 1 is an example of a tracing taken on July the 13th. It shows a regular radial pulse with a ventricular type of venous pulse. On July the 15th .06 grains of atropine sulphate were given subcutaneously in three divided doses at intervals of a quarter of an hour. This produced well marked atropine effects on the mouth and pupils, but the pulse remained absolutely uninfluenced. On this date the condition was therefore either one of complete heart-block with auricular fibrillation or one of complete heart-block with auricular waves too weak to register themselves. On July the 20th the pulse was distinctly slower than it had been, but it was still quite regular. Fig. 2 is a tracing taken on this date, and shows the presence of distinct and regular *a* waves. The auricle was beating at a rate of 70.5 beats a minute, and the ventricle at 37.5. Fig. 3 taken on July the 22nd shows the same condition, but the ventricle was beating slightly faster. The condition was now one of complete heart block with a normally acting auricle. The pulse continued regular till September the 2nd, and numerous tracings taken during this period were all similar to Fig. 2 and 3. On September the 2nd it was noted that the pulse was distinctly irregular. Fig. 4 is a tracing of this irregularity, and shows that it was due to mixed responses,^{1 & 2} the block having become incomplete.

The first four cycles are responses of ventricle to auricle, the heart beating with a 3 : 2 ratio. The *a-c* interval of each second effective auricular contraction is much increased. This is followed by a blocked auricular systole, and this in turn, by an effective auricular systole with an *a-c* interval of rather less than one-fifth of a second. Owing to the increase of the *a-c* interval in the second cycle, the radial beat is delayed with the result that



Fig. 1. Lower tracing radial, upper tracing jugal. Radial quite regular, venous tracing of the ventricular type. The time marker shows one-fifth seconds in all the tracings.

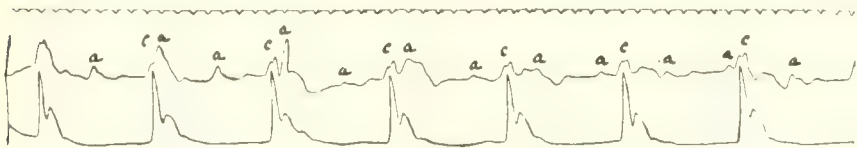


Fig. 2. Lower tracing carotid, upper tracing jugal. Complete heart-block. Auricular rate 70.5, ventricular 37.5 a minute.

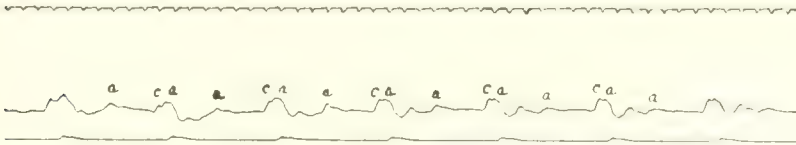


Fig. 3. Lower tracing radial, upper tracing jugal; similar to Fig. 2 except that the ventricular rate is 42.8.

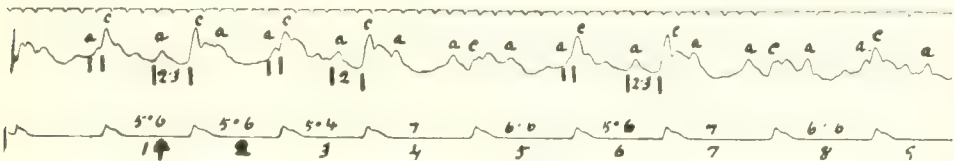


Fig. 4. Mixed responses. Lower tracing radial, upper tracing jugal. The figures above the radial tracing represent the duration of the pauses in one-fifth of a second, the figures below the numbers of the cycles. The arrow below the first cycle indicates the point at which radial beat No. 2 was due. The first four ventricular beats are in response to auricular stimuli; the 5th and 8th are spontaneous ventricular contractions; the 6th, 7th and 9th are responses to the auricle. An objection to this interpretation is the shortness of the *a-c* interval of cycle 6. An alternative explanation is that cycles 5 and 8 are responses to auricle and that cycles 6 and 9 are spontaneous ventricular contractions. If, however, the idio-ventricular rhythm is 6.6 one would expect a spontaneous ventricular contraction to terminate cycles 4 and 7, and this explanation also fails to account for the length of the *a-c* interval of cycle 7.

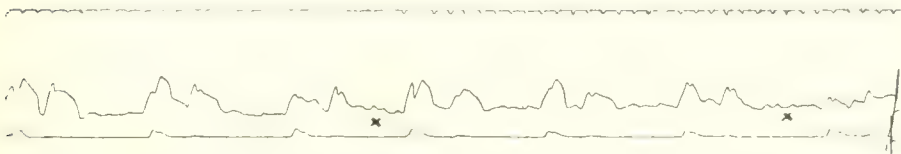


Fig. 5. Lower tracing radial, upper jugal. The regular *a* waves have disappeared. Coupled rhythm with unequal pauses following the extrasystoles is present. At X there are small waves during diastole.

the pause due to the succeeding blocked auricular systole is much shorter than it would otherwise be. The second radial beat is due at the spot marked with an arrow in Fig. 4. In the fourth cycle the *a-c* interval is only increased to two-fifths of a second instead of $\frac{2}{3}$ ths as in the second and seventh cycles, and the pause preceding it is thus only $\frac{1}{5}$ th in place of $\frac{2}{5}$ ths. The fourth cycle is terminated by a spontaneous ventricular beat, and is followed by a pause of seven-fifths of a second, which is exactly equal to the idio-ventricular pause in Fig. 3. The beats terminating cycles 5 and 6 are responses to the auricle, the *a-c* interval of 7 being again increased to $\frac{2}{3}$ of a second. Cycle 8 is due to a spontaneous ventricular beat, and cycle 9 is in response to an auricular contraction. Fig. 5 was obtained a few minutes after Fig. 4, the patient in the interval having been made to walk up a flight of stairs. The radial tracing shows a bigeminal pulse, the extrasystoles being followed by quite unequal pauses. The regular *a* waves have disappeared from the jugular tracing and during diastole numerous small waves similar to those found in auricular fibrillation are seen. Here and there the bigeminal action of the heart was interrupted by several consecutive extrasystoles. On September the 5th the pulse was again quite regular except that every third or fourth beat was premature. Fig. 6 taken on this date shows that the auricle was again acting normally. The premature beats were responses to every fifth or seventh auricular stimulus.

On September the 10th the block was again complete and the auricle was acting normally. The patient went home on September the 20th and returned to hospital on October the 24th. On re-admission the ventricle was beating at the rate of 26 a minute. It was, for the most part, quite regular but extrasystoles followed by pauses exactly equal to the ventricular rate, occasionally occurred. Fig. 7 was taken on this date, and shows the first four beats followed by extrasystoles. This was quite exceptional, and long portions of the tracing were quite free from extrasystoles. There is no trace of *a* waves. The patient died next day.

On admission to hospital the condition was one of complete heart-block. The block later became incomplete, but for some time before death it was again complete. The auricular action during the greater part of his first stay in hospital was normal. For the seven days following his first admission to hospital and for the short period immediately before his death, during which he was under observation, there was no sign of co-ordinate contraction of the auricle. The *a* waves also disappeared as a result of exercise on September the 2nd. Unfortunately as no electro-cardiograms were taken we have no positive evidence of auricular fibrillation. As, however, the *a* waves were always definitely present or definitely absent, and as at the autopsy the right auricle was found to be greatly hypertrophied, the probability is great that the absence of the *a* waves was due to temporary fibrillation of the auricles, and was not merely the result of weak co-ordinate auricular contractions. The small waves seen in Fig. 5 are also strongly suggestive of auricular fibrillation.

Autopsy.

Permission to examine only the heart was granted. The heart was hypertrophied and dilated. The pericardium was normal. There was a moderate deposit of sub-pericardial fat. The right auricle was slightly dilated and markedly hypertrophied. After fixation in formalin its wall measured at its maximum fully $\frac{1}{4}$ inch in thickness. The *taenia terminalis* was markedly hypertrophied. The appendix contained a firm thrombus. The coronary sinus was not dilated. The right ventricle after fixation measured four inches from base to apex. Its wall, at its thickest part

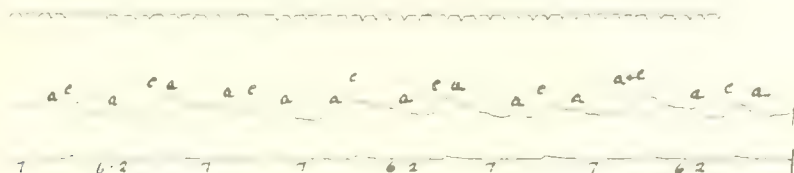


Fig. 6. Lower tracing (radio, upper jugular). Mixed responses, every fifth auricular contraction is conducted to the ventricle.



Fig. 7. Lower tracing (2). Apex lead, upper jugular. Complete heart block. The first four beats are followed by extrasystoles succeeded by pauses exactly equal to the pre-ventricular pauses of other causes.

measured $\frac{3}{8}$ inch in thickness. The tricuspid and pulmonary valves were normal. Except for an unusual hardness of the tissues, no definite changes could be made out in the region of the A-V bundle. The left auricle was slightly dilated and hypertrophied, its wall measuring at its thickest part $\frac{1}{8}$ inch. A rounded atheromatous patch with a diameter of $\frac{3}{4}$ inch was present on its inner wall. This appeared to be an extension of the marked atheromatous condition found in the aorta. The left ventricle measured $3\frac{1}{2}$ inches from base to apex, the thickness of its wall varied from $\frac{1}{2}$ to $\frac{3}{4}$ of an inch. The mitral valve, except for some thickening of the free margin of the anterior flap, was normal. The whole of the ascending portion of the aorta was slightly dilated, extremely atheromatous and studded throughout with dense calcareous patches. The bases of the aortic valves were all much thickened and nodular. The opening of each coronary artery was surrounded by calcareous plates and the lumen was diminished. The coronary arteries were both markedly thickened and nodular, this being most marked in the interventricular branch of the left coronary artery.

For microscopical study blocks of tissue were taken from the heart as follows:

1. The A-V junction containing the A-V node, the main stem and branches of the A-V bundle.
2. The region of the sino-auricular node.

3. Portions of the right auricle (*a*) at the junction of auricle and superior vena cava to the right of the sino-auricular node : (*b*) at the coronary sinus and (*c*) on the anterior aspect of the auricle.
4. Portions of the left and right ventricles and left auricle.
5. Papillary muscle from the right and left ventricles.

1. *The A-V junction.* The block excised was that recommended by Keith, the auricular end commencing just to the left of the coronary sinus. As the tissue felt hard it was decalcified for six hours in hydrochloric acid and embedded in one block. On attempting to cut this block it was found that there was still a considerable amount of calcareous matter present, and the block was again decalcified in nitric acid and re-embedded. Owing to the prolonged treatment during two decalcifications and embeddings a considerable amount of shrinkage took place in the block. Sections at right angles to the long axis of the block were cut 15 micra in thickness and every sixth section kept and stained with hæmatoxylin and eosin. The block was cut from the auricular end, but owing to the marked alterations in the parts it is more convenient to describe the bundle from its ventricular end backwards to the auricle.

Section 1116 shows that the bundle has left the membranous septum. The left branch of the bundle is seen as a well developed structure lying immediately below the endocardium of the left ventricle. Apart from a certain number of the muscle cells being swollen, and containing vacuoles surrounding the nuclei, the bundle appears to be normal. No fibrous infiltration is visible. The right branch of the bundle cannot be identified in the ventricular muscle.

In Section 1110 a portion of the left branch of the bundle appears in the left side of the membranous septum. It shows changes which will be described later in detail.

Tracing the sections backwards, the altered bundle becomes more and more visible in the membranous septum. In section 998 it is a very definite structure and shows a division into two horns.

Section 924 shows, under a low power, a mass of tissue fairly sharply demarcated from the remainder of the membranous septum, and lying rather to the left of the septum. It is roughly triangular in outline, but there is a distinct indication of a division into a right and left branch. The mass has quite a different colour tone from the rest of the membranous septum : it occupies the position and has about the normal size of the bundle in this situation. A large central artery has its lumen completely obliterated by cellular deposit, though the elastic lamina is intact. With a higher power the main bulk of this tissue consists of a meshwork of fibrous tissue in which are areas having a distinctly different staining reaction. These stain pinkish brown, while the connective tissue is coloured a definite pink. Throughout these pinkish brown areas there are numerous cells with the outline and colour of muscle cells. The vast majority of these cells show no nuclei, but in a

few of them definite nuclei can be seen. These cells are, in our opinion, the altered muscle cells of the bundle.

Tracing the bundle backwards it becomes more and more replaced by well staining fully-formed fibrous tissue. The obliterated artery continues to form a landmark in the sections.

This condition continues until the upper part of the septum is approached and here it is gradually replaced by a new type of tissue. In section 702 the central artery begins to show a small central passage. The fibrous tissue is becoming much more cellular and there is still a trace of altered bundle tissue.

Section 562 shows the artery of the bundle lying along the right side of the central fibrous body. The artery now shows a definite lumen, but in place of the altered though still recognisable bundle which is seen in previous sections, its place is completely occupied by a small round celled deposit. This deposit consists for the most part of fibroblasts, but there are also many lymphocytes, plasma cells and a few multinuclear giant cells of the type met with in the infective granulomata. A large number of newly formed blood vessels are present among the cells. In addition to completely destroying the region of the bundle this deposit of cells infiltrates the central fibrous body.

Passing still further back towards the coronary sinus the cellular deposit gradually becomes more fibrous. The auricular muscle in the central portion of the interauricular septum is completely destroyed by a dense band of fibrous tissue containing here and there masses of round cells. This fibrous tissue also invades and destroys to a very large extent the muscular tissue below the right auricular endocardium. Here and there, however, there are definite bundles of more or less altered muscular tissue, which may represent portions of the A-V node; but owing to the conspicuous atrophic changes in the ordinary muscle fibres in the neighbourhood no definite statement can be made as to this.

2. *The sino-auricular node.* Serial sections were cut through the sino-auricular node. Unfortunately, the sections containing the right pole of the node were destroyed by accident. The left pole and the central portions of the node are well developed and, apart from a very slight thickening of the walls of the central artery and the presence here and there of very small accumulations of small round cells, are normal. The node was not stained to show fatty degeneration.

3. *The right auricle.* Sections from the highest part of the auricle to the right of the sino-auricular node show comparatively large and dense accumulations of small round cells. These are most conspicuous immediately below the endocardium, but are also present here and there throughout the muscle wall. Fig. 13 is from this region.

Sections from the neighbourhood of the coronary sinus show very marked fibrosis of the interauricular septum with numerous calcareous deposits. The vessels show marked endarteritis obliterans. Fig. 14 is

from this region. Sections from the anterior wall show great hypertrophy of the muscular tissue. There is no fibrosis or small celled infiltration. Stained with Scharlach R., a few fibres show fatty degeneration.

4. Sections of the left ventricle show, when stained with Scharlach R., a considerable amount of fatty degeneration. There is no fibrosis and no infiltration with round cells. The right ventricle is in a similar condition, but the fatty degeneration is distinctly less marked. Sections from the anterior aspect of the left auricle show no fibrosis and no infiltration with round cells. A few fibres show fatty degeneration.

5. The papillary muscle from the right and left ventricles shows very definite fatty degeneration, especially on the left side.

To sum up the pathological changes, the heart shows hypertrophy and dilatation of all its chambers with conspicuous changes in the aorta and coronary arteries. There is complete destruction of a large part of the main stem of the auriculo-ventricular bundle with advanced degenerative changes in the remaining portions of the main stem. The sino-auricular node is practically normal. The auricular tissue to the right of the sino-auricular node shows extensive infiltration with round cells. The interauricular septum near the coronary sinus shows marked fibrosis and calcareous degeneration. There is slight fatty degeneration of the right and left auricles and more marked fatty degeneration of the muscle of both ventricles. In our opinion the changes observed point to a syphilitic origin.

Summary and Conclusions.

A case of heart-block is described. The block was at first complete but seven weeks before death, it became incomplete for several days. During the greater portion of the time the case was under observation, the auricular action was normal, but on three occasions there were attacks of auricular fibrillation. During two of these attacks, the heart-block was complete and the slow and regular idio-ventricular action remained unaltered. On the third occasion the attack of auricular fibrillation was produced by exercise while the heart block was incomplete. The ventricle then showed a slow irregular bigeminal action exactly similar to that of an uncomplicated case of auricular fibrillation while under the action of digitalis. At the autopsy complete destruction of a large part of the main stem of the *A-V* bundle was discovered. As this destruction was due at the parts, where it was complete, to purely cellular elements, fibroblasts, lymphocytes, &c., and at other parts to fully formed fibrous tissue, it is clear that the pathological process was progressive and that the complete destruction of the bundle must have been of recent date. The reduced ventricular rate during the periods of auricular fibrillation can only be referred to the changes in the *A-V* bundle demonstrated post-mortem.

We are much indebted to Dr. Duncan for the micro-photographs.

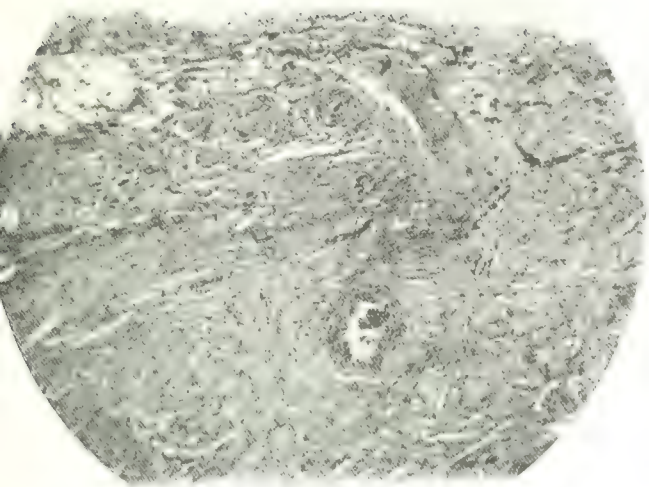


Fig. 12.

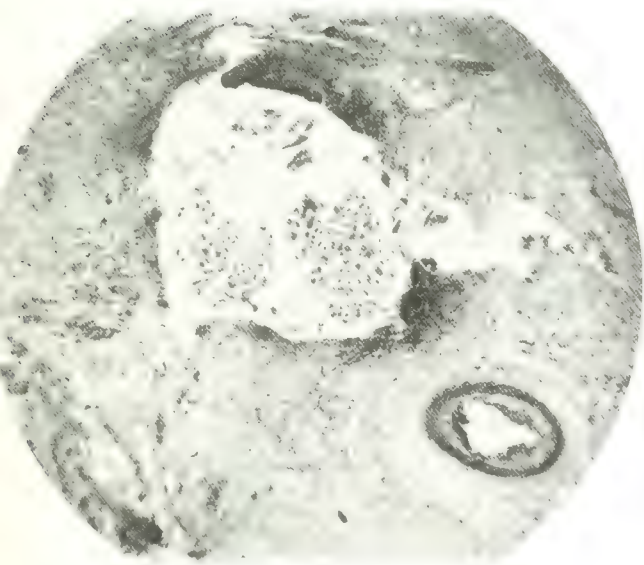
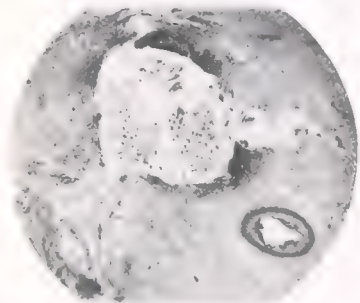
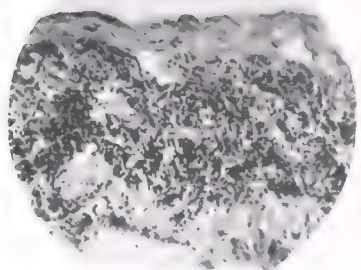
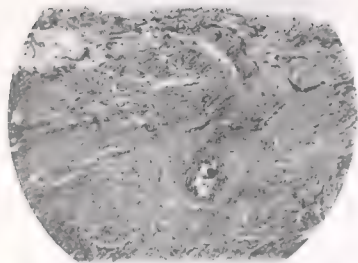
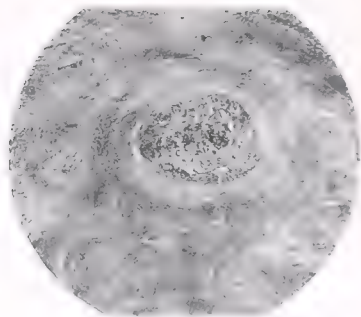


Fig. 14.



STIMULATION OF THE ISOLATED VENTRICLE, WITH SPECIAL REFERENCE TO THE DEVELOPMENT OF SPONTANEOUS RHYTHM.

By ARTHUR R. CUSHNY.

THE great majority of the irregularities of heart hitherto examined arise from the development of spontaneous contractions in parts of the heart in which the generation of rhythm is normally in abeyance. The chief other causes which have been recognised are abnormal conductivity and the anomalous contraction which gives rise to pulsus alternans. The development of spontaneous activity in ordinarily passive parts of the heart is therefore of great interest from the clinical standpoint to-day as it has always been from the physiological. Many of the conditions underlying rhythmic activity, such as temperature, nutrition, have been the subject of innumerable investigations, but the development of spontaneous rhythm in a normally passive part of the heart still remains quite obscure.

A new method of approaching the subject seemed to me to be offered by an observation of Erlanger and Hirschfelder,¹ who in the course of their work on heart-block observed that if the spontaneous rhythm of the isolated mammalian ventricle is accelerated by a series of rapid electrical shocks, there follows afterwards a period of slow contractions of the chamber very similar to that observed immediately after severing it from the auricle by dividing the auriculo-ventricular bundle. This slow rhythm then gives way gradually to the ordinary rhythm of the isolated ventricle. Here it seemed the generation and extinction of spontaneous rhythm might be studied under controllable conditions. I have therefore performed a number of experiments on the effects of stimulation of the mammalian ventricle separated from the auricle by division of the His' bundle.

Most experiments were made on the cat's heart, a few on the rabbit's. The animal was killed by a blow on the head and immediately bled from both carotids. The heart was excised and perfused with Locke's solution through the aorta in the usual manner. After normal contractions had been developed, the right ventricle was opened and the bundle cut as described by Cullis and Dixon.^{2*} The contractions were recorded by a lever which

¹ I am much indebted to Miss Cullis for kindly showing me the details of the method.

was attached to the apex of the heart by a thread and hook in the usual way. The ventricle was stimulated by means of fine wires hooked into it and leading from a secondary coil. In the primary circuit there was inserted in addition to the signal, key, &c., a rotating interrupter driven by a small electric motor furnished with screw reducing gear and working through a pair of gradually tapering cone pulleys, through which the rate of the stimuli could be very exactly graduated.

When the ventricle was beating automatically, and its usual slow rhythm was accelerated by a series of shocks at a more rapid rate, it did not reassume its original rhythm when the artificial stimulus was withdrawn, but as a general rule remained quiescent for some time and then recommenced beating very slowly, and sometimes irregularly, gradually accelerating its rhythm until it resumed its original rate before stimulation. The initial pauses are exactly similar to those which occur on section of the auriculo-ventricular bundle, as Erlanger and Hirschfelder pointed out.

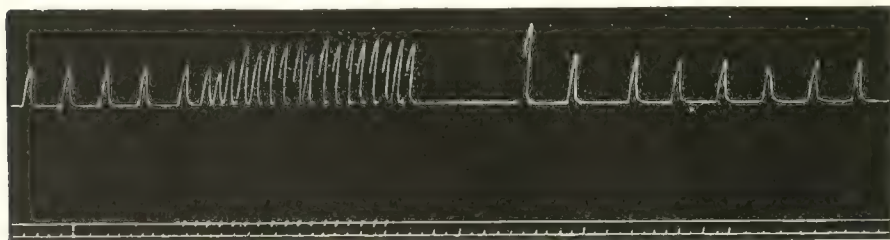


Fig. 1. Upper line, ventricular tracing; middle, stimulation signal; lowest, time in seconds. Stimulation by electric shock for 8.3 seconds.

The interval preceding the first spontaneous contraction is often of very great length: for example, in a ventricle whose rate before stimulation was 30 per minute, this interval in one instance extended over 20 seconds. In another instance a ventricle beating normally at 120 per minute stood still for $7\frac{1}{2}$ seconds; but as a general rule it was much shorter. The interval between the first and second contractions was usually somewhat shorter than that preceding the first but not infrequently was actually longer. Erlanger and Hirschfelder seem to have found the second interval longer than the first in a larger proportion of their experiments. The succeeding intervals became progressively shorter as a general rule but occasionally the third pause was the longest of all. And in some experiments after the rhythm had definitely begun to accelerate, for example after 6 or 8 spontaneous contractions, a pause of very considerable length intervened.

The phenomenon is a very definite one and occurs only in the spontaneously beating ventricle; as long as the ventricle beats in response to auricular impulses the first pause after the ventricular stimulation is less than two normal pulse intervals, and the second interval is of normal length.

The time elapsing before the slowly accelerating ventricle reaches its previous rate varies greatly in different hearts and, in the same heart, in successive observations. Sometimes the normal rate is resumed in the course of ten seconds after the cessation of the artificial stimuli; in other instances several minutes are required; and sometimes the original rhythm is not reached in the course of the experiment. These variations were found to be dependent in part on the method of stimulation and in part on the condition of the heart at the time. The latter factor is obscure, but some of the causes which promote this hypotonic condition of the ventricular pacemaker were ascertained.

(a) Condition of the heart in general.

The pause and slowing were generally more marked and more persistent in the later phases than in the beginning of my experiments, as in those of Erlanger and Hirschfelder. As the energy of the heart decreases the results of the accelerated rhythm become greater and a longer interval must be allowed to obtain the return of the rhythm prevailing before the interference.

In fact, in the earlier part of an experiment the phenomenon may not be at all well marked, the ventricle resuming its previous rhythm after two or three beats slightly slower than usual. Or the acceleration may be followed by a prolonged slow stage which gradually passes into the normal rhythm (Fig. 2) without any such pauses as are shown in Fig. 1 being developed.

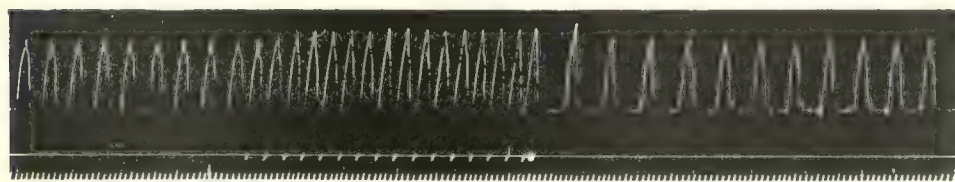


Fig. 2. The original rhythm of 63 per minute was artificially raised to 90 during 10 seconds. The rhythm afterwards was regular but slow with a very gradual acceleration, the first ten contractions being at the rate of 45.5 per minute, the next ten at the rate of 53.5 per minute. Time in one-fifth seconds.

The reaction illustrated in Fig. 2 is merely a lower form of that seen in Fig. 1, however, for it tended to change into the phase of prolonged pauses as the experiment continued and the heart became more exhausted, and the

other factors which exaggerated the pauses also tended to change the slowing to the pause phase. Thus the slow regular rhythm of Fig. 2 occurred especially when the rate of stimulation was not much in excess of the spontaneous rhythm, and a more rapid series of shocks often elicited distinct pauses.

The more marked pauses may be elicited very readily in any perfused ventricle by allowing the temperature of the solution to sink to about 32-34° C. before inducing the artificial rhythm. And, if the reduction of temperature has not lasted too long, the more marked effects seen at the lower temperature disappear again on raising the temperature to 38° C. and again stimulating.

Another method of eliciting distinct pauses in a strongly contracting heart is by reducing the oxygen in the perfusing fluid. In my earlier experiments the fluid was thoroughly oxygenated before the perfusion began, but no oxygen was passed through afterwards. This is sufficient to maintain the rabbit's heart in fair condition, and only the less marked forms of the failure of rhythmicity were seen in the earlier part of experiments on those animals. The cat's heart requires a large supply of oxygen apparently, for the pauses were very marked and the general condition of the heart was much less favourable than in the rabbit, unless oxygen was bubbled through the fluid throughout the perfusion.

The effects of reducing the oxygen of the Ringer's solution on the recovery of the ventricle from artificial stimulation are shown in Experiment 1.

Experiment 1. A cat's heart was prepared in the way described. The spontaneous ventricular rhythm was 45-48 per minute, *i.e.* 5 beats occupied 6.2-6.7 seconds. It was stimulated with electric shocks at the rate of 168-170 per minute for 6.5 seconds and this was followed by some slowing, as is seen in the table below, which gives the time occupied by the first five contractions after the stimulation ceased. The ordinary oxygenated Ringer's solution was now replaced by some which had been recently boiled to expel the oxygen, and each five minutes as this was being perfused, the ventricle was again stimulated by electric shocks at the same rate and of the same duration. After the boiled Ringer's solution had been perfused for 15 minutes it was again replaced by the original oxygenated solution and five minutes later the ventricle was again stimulated as before. It must be added that the boiled Ringer's solution was not completely free from oxygen when it reached the heart as it passed through narrow tubes whose walls were covered with bubbles of oxygen liberated from the oxygenated solution previously used; but the amount of oxygen was undoubtedly much reduced. The table gives the time occupied in the first five beats after the stimulation in each case, contrasted with the time of five beats before stimulation. The rate of the ventricle was not diminished by the partial asphyxia in this case.

Normal rate, 5 beats in 6.2-6.7 secs.

After stimulation, 5 beats in 7.5 secs. in oxygenated solution.

5	9.3	after 5 mins. asphyxia.	
5	16.3	10
5	20.0	15
5	13.9	5	oxygenated solution.

A depressed (hypodynamic) condition of the ventricle is therefore one of the factors which favour this failure to recover from acceleration. This depressed condition may be elicited by cold, by asphyxia, or by



Fig. 3. Upper line ventricular tracing, middle line time in seconds, lower stimulation signal. Slight alternation before stimulation becomes very marked during the acceleration and in the beginning of the slow beats. Staircase phenomenon during the acceleration. Subsequent slowing not very marked.

prolonged exposure to the conditions of the experiment. It was of interest to determine whether the condition of the heart in which this failure of the rhythmicity is marked is the same as the hypodynamic state in which occurs the curious alternation of contractions giving rise to *pulsus alternans*. I have looked through my tracings to find whether alternation is generally more marked in the cases in which the impairment of rhythmicity is very evident, and the general result is that while alternation is very common during the phase of acceleration, it is not generally more marked in the experiments in which the most prolonged pauses occurred, and is sometimes entirely absent in these; in other tracings well marked alternation of the ventricular contractions occurred during the artificial rapid rhythm without the pause phenomenon being at all well marked. (Fig. 3). The abnormality underlying alternation may therefore be present along with that which favours the failure of rhythmicity, but they may occur separately and are not identical.

(b) *Number of stimuli and duration of stimulation.*

Erlanger and Hirschfelder found that the rate and duration of the artificial stimulation influenced to a great extent the duration of the succeeding pause, and here again my results are in accord with theirs, as is seen from the following experiment.

Experiment 2. Cat's heart, ventricle beating 36 per minute. Artificial stimuli at the rate of 132 per minute. Interval between two contractions is normally 1.6 seconds.

Duration of stimulation in secs.	Number of artificial beats.	Duration of first pause in secs.	Duration of second and third pauses together in secs.	Interval in secs. between end of stimulation and resumption of normal rate.	Number of beat after end of stimulation or before resumption of normal rate.
9.0	22	7.7	5.7	35	14
4.5	10	3.5	5.0	25	11
1.5	4	2.0	3.5	11	6
—	1	1.8	norm.	—	4
5.0	11	3.5	5.2	25	13
1.0	3	2.0	3.2	7	3
10.0	24	7.8	5.5	37	16
—	2	2.0	3.5	5	2
—	1	1.8	norm.	—	—
—	2	2.2	..	5	3
—	2	2.0	3.2	8	5
2.5	5	2.4	3.7	15	9

In this experiment the duration of the pause before the first spontaneous beats and the intervals before the second and third beats are seen to be roughly proportional to the number and duration of the artificial stimuli.

The interval during which the rhythm remains slow, *i.e.*, before the normal rhythm is regained, is also dependent on the duration of the artificial rhythm. No absolute parallelism is present in any experiment because, as will be shown, a previous period of stimulation often has effects lasting over many minutes, but the numbers are sufficient to demonstrate the relation and permit the inference that the effects of an artificial rhythm are to depress the rhythmicity of the automatic ventricle, and the degree of depression varies with the duration of the artificial rhythm. It is of interest to note that in this experiment a single extrasystole causes a very slight depression, the interval between the extrasystole and the succeeding beat being 1.8 seconds, while the normal period is 1.67 (compare Fig. 4). This I have noted repeatedly although as a general rule there is no such delay, the interval between the extrasystole and the next contraction generally being the normal pulse period. In other words, in the spontaneous ventricle an extrasystole is not followed by a pause as a general rule, but in some cases the next spontaneous contraction may be delayed, *i.e.*, there may be an imperfectly "compensatory" pause. In my experience this pause has occurred generally in hearts which have been under observation for some time and in which the slow recovery from artificial rhythm has been well marked.

In a previous experiment³ on the spontaneously beating ventricle of the dog *in situ*, I described a similar delay after an artificial stimulus (*i.e.*, there was a partially compensatory pause), and similarly on stimulating in the neighbourhood of the great veins there was the same delay in the appearance of the succeeding contraction: it is generally stated, however, that in spontaneously beating parts of the heart there is no compensation.

the interval between the extrasystole and the next normal beat being the normal pause period. As far as the ventricle is concerned this is true for many hearts, but there are conditions in which the spontaneous beat of the ventricle is delayed after an extrasystole and there is thus "partial compensation." If this may be extended to the normally automatic area of the heart in the Keith and Flack node, an extrasystole may ordinarily be followed by a normal interval without any attempt at compensation, but in depressed conditions of the heart, there may be some delay here also.

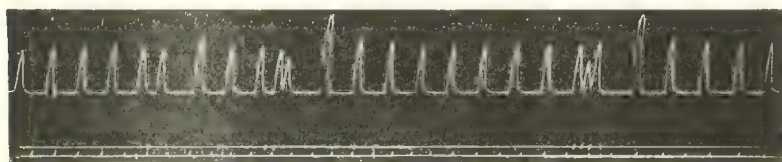


Fig. 4. Stimulation with one, two and three shocks. Time (lowest line) in seconds. Increased pause after one stimulus. Slowing extending over several beats after two or three beats in accelerated rhythm.

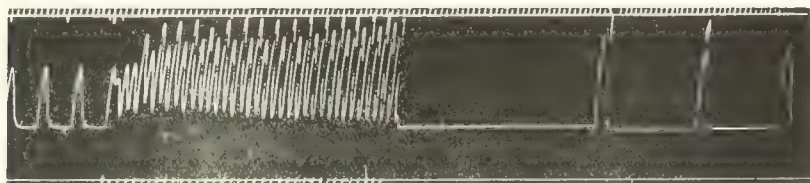
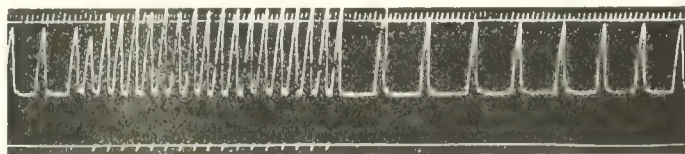


Fig. 5. Effects of stimulating the ventricle at the rates of 112 per minute (*a*), and 230 per minute (*b*). An interval of five minutes between (*a*) and (*b*). Time in one-fifth seconds, highest line.

This may perhaps help to explain certain difficulties that have arisen in the interpretation of pulse tracings in man in regard to extrasystoles of the auricle, in which the pause seems to be longer than would be accounted for by the view which I suggested some years ago. In this I assumed that the interval between a premature stimulus of the pacemaker and the normal stimulus following was exactly the interval between two normal pulses; the partial compensation which occurs after an auricular extrasystole was explained by the stimulus passing backward to the pacemaker and discharging it, the next impulse from it arising at the normal interval and descending

to the auricle. The interval between the beginning of an auricular extrasystole and the following beat would thus exceed a normal pulse interval only by the time required for an ascending impulse to reach the pacemaker and a descending one to reach the auricle. As a matter of fact the interval after an auricular extrasystole is often longer than would be easily accounted for on this view, but if the impulse from the auricle not only discharges the pacemaker, but also in certain conditions depresses it, it seems possible to rehabilitate the view. And that this may occur is suggested on the analogy of the spontaneously beating ventricle in the present series of experiments.

(c) *Rate of stimulation.*

The rate of the artificial rhythm influences to a marked extent the character of the following contractions. (Experiment 3, and Fig. 5 (a) and (b).)

Experiment 3. Cat's heart. Divided bundle. Normal rate of ventricle 50 per minute, *i.e.*, pulse interval = 1.2 seconds. Stimulated in each case for 10 seconds.

Rate of stimulation.	Duration of first pause.	Duration of first and second pause.	Duration of first five pauses.
15 in 10"	1.4"	2.5	6.6
15 ..	1.6"	3.0	7.2
18 ..	1.6"	3.4	8.4
24 ..	6.2"	10.2	16.0
32 ..	7.8"	12.2	—
22 ..	1.8"	3.6	10.2
36 ..	9.4"	14.0	—

Here a very definite decrease in the power of recovery is seen with each successive increase in the rate of stimulation, though it is difficult to reach absolute figures from the fact that repeated stimulation at short intervals in itself decreases the rhythmicity, as will be discussed later. Not infrequently a moderate acceleration induced merely a slight slowing, as in Fig. 2, without pauses, while a greater acceleration was followed by distinct pauses and irregularity, and every gradation between mere slowing and distinct standstill could sometimes be elicited by changing the rate of the artificial rhythm.

The smallest acceleration which was found to exert this depressing effect was of interest, but varied in different hearts and in the same heart at different stages of the experiment. Very distinct slowing or pauses may often be elicited by accelerating the rhythm by 50 per cent., and late in the experiment prolonged acceleration of about 10 per cent. may elicit the phenomenon. The degree of acceleration necessary thus varies with the duration of the artificial rhythm and also with the condition of the heart.

The acceleration necessary to induce subsequent slowing and pauses may in fact be taken as a rough gauge of the condition of the heart, the better the general nutrition the greater and longer the acceleration which can be borne without serious derangement of the rhythmicity subsequently.

In man complete auriculo-ventricular block may exist with fair general health, but in many cases of block there are phases of extreme slowing which may induce the Stokes-Adams syndrome. In one case* the extreme slowing was always preceded by a period of acceleration, and the similarity to the automatic ventricle in my experiments is striking. The inference may perhaps be drawn that the extreme slowing in man in complete block is not only of gravity in itself from the imperfect circulation but also as betraying a seriously impaired condition of the ventricular nutrition. In one of my tracings a sudden acceleration from some unknown cause occurred and was followed by a period of slow pulses (Fig. 6), and in another the acceleration induced artificially continued for some time after the electric shocks had ceased and again a pause followed. This suggests that a spontaneous acceleration if marked may be sufficient to induce the same imperfect rhythmicity as I have described.

In this connection it may be added that the effects of electrical stimulation are the same wherever the electrodes are applied. In several experiments one pair of electrodes was attached as near as possible to the cut bundle, another pair to the apex, and series of shocks were alternately passed through the bundle and through the apex, but no difference could be detected in the effects.

Change in the strength of the shocks has no influence on the phenomenon. The minimal strength which is capable of inducing an artificial rhythm is as effective in inducing the pauses as much more powerful ones. Shocks which do not suffice to cause artificial rhythm are without effect on the rhythmicity.

The factors determining the appearance of these pauses so far observed are then (*a*) the condition of the heart in general, its temperature and oxygen supply, and the length of time it has been exposed, (*b*) the duration of the stimulation, and (*c*) the rate of stimulation. In one experiment these did not seem sufficient to explain the features observed, for several times successive stimulation of the same duration and rate was followed alternately by well marked pauses and by merely slight slowing, and there was not any appreciable difference in the heart's nutrition to explain these.

Is the phenomenon inhibitory in nature?

Acceleration of the rhythm of the spontaneously beating ventricle thus induces a condition in which the rhythm is temporarily in abeyance. It was of importance to determine what is the condition of the ventricle during this period of inactivity. First it had to be determined if the stoppage was

* See Lewis and Cohn (as yet unpublished).

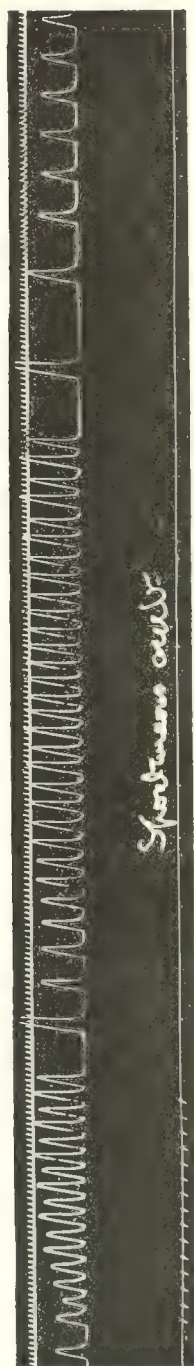


Fig. 6. Spontaneous acceleration of the ventricle leading to slow rhythm. Time in one fifth seconds, upper line.



Fig. 7. Successive stimulations of the ventricle at short intervals at the same rate and of the same duration. Increasing depression of the rhythmicity.

of the nature of inhibition, and several experiments were performed in which atropine was added to the perfusion fluid to the amount of 0.01 per cent. without removing the slowing. This is far more than sufficient to paralyse the inhibitory nerves. And in many features the phenomenon does not resemble the effects of inhibition as ordinarily understood. Thus if the inhibitory apparatus were stimulated by the electric shocks, the effects would be most marked from a short series of stimulations, while prolonged excitation would tend to fatigue the inhibition. But, as has been stated, the longer the stimulation is applied the more marked the subsequent slowing. The strength of the shocks might also be expected to be of importance, and stimulation at a strength below that necessary to cause rhythm might induce the slowing. Moreover even strong shocks applied at the same rate as the normal ventricular rhythm induced no slowing or pauses. On these grounds the inhibitory mechanism may be absolved from responsibility for the phenomenon under examination.

Excitability and contractility during pause.

During the longest pauses the muscle remains capable of contraction on stimulation, and in fact responds with an abnormally powerful beat, so that the slowing is obviously not due to exhaustion of the contractile elements.

The excitability of the heart by electrical stimulation also remains unimpaired during the pause. This was ascertained in a number of experiments in which the minimum shock to which the ventricle responded during spontaneous rhythm was measured, a rapid artificial rhythm was then elicited and during the subsequent pause the threshold shock was applied. The minimal shock was found by gradually approaching the secondary coil from which wires led to the electrodes in the heart, until rapid shocks were just sufficient to cause irregularities in the form of extrasystoles. This point ascertained, the current was strengthened and a fast rhythm was elicited, and during the subsequent pause either single shocks or a series of shocks of the minimal strength were sent through the ventricle. The heart responded to the threshold stimulus as before, but failed to contract if the shock was reduced further in strength. For example, in one experiment, stimulation with the coils at 105 mm. distance was sufficient to cause an accelerated artificial rhythm, while stimulation at 110 mm. distance was ineffective. A rapid series of shocks, applied at 80 mm. for 10 seconds, was followed by very marked pauses. After an interval for recovery, rapid shocks at 80 mm. distance were again given for 10 seconds, and then the strength was reduced to 105 mm. which maintained the same rapid rhythm. Pauses occurred, however, as before as soon as the distance was increased to 110 mm. And when the rapid rhythm was induced at 80 mm. distance and the coils were then withdrawn to 110 the pauses occurred as if the shocks had ceased altogether. The same results followed if the pause were allowed to develop before the threshold shock was applied.

The close approximation during the pause to the normal excitability was especially marked in some cases in which shocks of a certain speed and strength alternately induced contractions and failed of effect owing to every second shock falling during the phase of lowered irritability from the preceding contraction. Strengthening the current then doubled the rate of beat, as each shock became effective. Thus in the above experiment when the coils were at 105 mm. distance, stimulation at the rate of 96 per minute gave a rhythm of 96 per minute, each shock being effective, while at 107 mm. distance the same rate of stimulation caused only 48 beats per minute, and at the distance of 109 mm., shocks had no effect whatever. During the pause following acceleration, the same values held, stimulation at 105 mm. distance causing a rhythm of 96, that at 107 causing one of 48, and stimulation at 109 failing to cause any movement or to interrupt the pause.

During the pause after acceleration the irritability of the ventricle therefore reaches the same threshold value as during its ordinary rhythm.

The same result may be reached by consideration of another observation. For if the excitability were exhausted by the series of artificial stimuli, the threshold stimulus would fail to maintain the accelerated rhythm after a time. In two experiments the minimal strength of shock necessary to elicit the rapid contraction was accurately determined, and this was then maintained for two minutes and five minutes without interruption. But the heart continued to respond to it at the end, and when during the succeeding pause the series of shocks was resumed, the ventricle responded again. Here again the excitability of heart muscle does not seem impaired by prolonged stimulation. On the other hand it does not seem to rise to an abnormal height during the pauses, for sub-minimal stimuli were not efficient at any time during the quiescence. It is of course possible that just before the spontaneous contraction there is a sudden access in the excitability of the ventricle, but there is no evidence of such a change in my work. It may be taken then that the excitability of the ventricle rises during the pause in the same way as after a normal contraction, reaches a maximum, and then remains with little change until the first spontaneous contraction. The latter cannot be regarded as the culmination of a gradually increasing excitability, for the latter has reached its maximum it may be as much as two seconds or more earlier. In other words the rhythmic stimulus arises in the heart by a different process of anabolism from that involved in the recuperation of the excitability to external stimuli. (See note p. 278.)

Fatigue of the cardiac functions.

When the connection between the auricle and ventricle is severed, so that the latter receives no further impetus from above, the ventricle after greater or less delay commences to beat spontaneously, as was shown by Gaskell for the cold-blooded heart and as has been recently developed by Erlanger and his collaborators and others for the mammalian heart. Gaskell

concluded that the ventricle is constantly capable of rhythm, but as its rhythmicity is of a lower order than that of the auricle and pacemaker, it normally has no opportunity of beating automatically because the spontaneous ventricular contraction is always anticipated by an external impulse reaching it from above. As far as I gather, his view is that the pacemaker dominates the heart simply by anticipating the spontaneous development of rhythm in the other parts; when the impulses from the pacemaker are cut off, the ventricle develops its own rhythm, at first slowly and then more quickly. My results reveal another factor in the process, for they indicate that the pacemaker not only anticipates the ventricular spontaneous beat but actively depresses the ventricular rhythmicity. The slowness of the earlier idio-ventricular beats after section of the bundle is due not merely to the ventricle gradually developing an unaccustomed function, but to its recovering from the state of depression to which it has been reduced by a life-long series of impulses from above.

This condition of depression in which the ventricular spontaneity is normally maintained by the dominant pacemaker and which may be induced by an artificial rhythm, resembles the phenomenon of fatigue of voluntary muscle. Thus its extent depends on the number and rate of the stimuli applied, it passes off slowly and may be renewed repeatedly.

There is no analogous effect on the contractility of the heart muscle, which, as is well known, is not weakened by prolonged activity, and whose strength may actually increase when the rhythm is accelerated. The excitability of the ventricle as measured by the minimal electric shock which arouses a contraction, also shows no cumulative depression in my experiments and thus resembles the contractility in its behaviour. In the case of the conduction of impulses there appears to be something of the nature of fatigue, for all the evidence from Gaskell onwards points to the view that when unusual calls are made on the impaired conduction power of the heart, there is a certain cumulative effect seen, the passage of one impulse causing unusual difficulty in the conduction of the following, and this increasing with each impulse until it culminates in the complete block of one impulse, which may be interpreted as complete fatigue of the conducting A-V fibres. On the other hand, where several contractions of the auricle fail to elicit more than one ventricular systole the efficient impulse may be held to fatigue the bundle to such an extent that it only gradually recovers. The conduction after an intermission is abnormally rapid, as the conductivity fibres recover from fatigue. The question arises whether the function of conduction like that of rhythmicity is normally kept in a state of submaximal activity, whether the bundle of His, for example, is in a constant state of partial fatigue. This may be the explanation of the distinct pause which occurs between the auricular and ventricular systole, but as intermissions are rare except in defective conductivity it is difficult to determine the question. The fact that even in imperfectly conducting hearts the auriculo-ventricular interval after a pause is shorter than that in normal hearts suggests however that

even in the normally beating heart the conductivity is partially fatigued by its exercise.

The fatigue of the rhythmic function in all parts of the heart except the pacemaker is of advantage in preventing spontaneous heterotopic contractions and preserving the regular sequence of the cardiac movements. The fatigue of the conducting fibres is of service in allowing the auricle to empty itself into a flaccid ventricle. When the conductivity is abnormally efficient and the ventricular contraction follows too soon on the auricular, the auricle has often to act against a contracting ventricle and some of the auricular contents are driven backwards into the veins instead of forward, with a corresponding waste of energy.

The function of conductivity like that of rhythmicity thus appears to be susceptible of fatigue such as is more familiar in striated muscle and nerve, while the excitability and contractility of the cardiac muscle seem immune to it.

The fatigue of the rhythmicity is remarkable in the fact that it arises not from the activity of this function in itself, but rather while it is in abeyance from the presence of extraneous impulses. Apparently it is elicited by the contractions of the muscle, not from the actual generation of rhythm, and this immediately suggests that the spontaneous rhythm fails after acceleration because the ventricular pacemaker is overwhelmed by the waste products arising from the contractions. As these metabolites are got rid of, the pacemaker regains its power of emitting impulses and the ordinary idio-ventricular rhythm is reinstated. This view is in accord with the modern view of muscular fatigue to which the exhaustion of rhythmicity shows strong analogy.

Another phenomenon with which it shows analogy is the apnoea which results from forced breathing and which has been ascribed by Haldane and Douglas to the excessive ventilation of the lungs reducing the proportion of carbonic acid in the blood. The results of the diminution of carbonic acid on the circulation and heart have been demonstrated by Henderson⁵ and by Jerusalem and Starling.⁶ It seemed possible that the excessive rate and the strong contractions of the heart during the acceleration might have the effect of more efficiently supplying it with oxygen and removing its metabolites, somewhat in the same way as massage, and that the pause of the heart might resemble that of the respiratory centre in apnoea.

In one experiment this mechanical effect of the acceleration was excluded as far as possible by shutting off the Ringer's fluid immediately before the acceleration was induced and comparing the effects with those of a previous acceleration induced in the ordinary way during perfusion.

	Rate before acceleration.	Rate during 15" acceleration.	Average rate of seven beats after acceleration.
Control	114 per minute	264 per minute	86 per minute
Ringer shut off	112 " "	264 " "	86 " "

In this experiment the removal of the products of activity by the perfusing fluid had no influence on the after effects of stimulation. If the Ringer's fluid is shut off longer, asphyxia slows the spontaneous rhythm and then acceleration is followed by much greater slowing. From this experiment the inference may be drawn that the acceleration does not act merely by improving the supply of oxygen and the removal of waste products by the perfusing fluid. It is possible that it may influence the nutrition indirectly by a sort of massage of the fibres and this may account for the increased height of the contractions as the acceleration is developed. But it does not seem likely that the subsequent pause is due to either the excess of oxygen or the diminution of metabolites. On the other hand the pause phenomenon seems opposed to Langendorff's view that the stimulus formation in the heart arises from the metabolites formed from its previous activity for these must be present in large amount after the acceleration.

Erlanger and Hirschfelder note that the second pause after the acceleration is often longer than the first, and this has not infrequently been the case in my experiments, although apparently not so often as in theirs. This might be interpreted as being due to the fatigue increasing for some time after the acceleration has ceased, but this is not the necessary inference. I would suggest that there are two opposing factors here, the one—the fatigue due to the acceleration—which delays the spontaneous rhythm, the other which favours it, and which may perhaps be the improved nutrition of the heart from the increased oxygen supply and the self-massage from the rapid and accelerated contractions during the stimulation. If the latter factor disappears more quickly than the fatigue the first pause may well be shorter than the second. The effect of oxygen on the rhythmicity has been illustrated already in Experiment 1, in which it was shown that the rhythm was restored much more quickly than during asphyxia. The effects of massage on the feebly beating heart were equally obvious, the rhythm accelerating for some time afterwards and the contractions gaining in strength.

The fundamental factor in the phenomenon under discussion is therefore the retarded rhythmicity. Instead of the energy for a spontaneous beat being accumulated in one second, it may require 2 or 20 or more seconds, and as the fatigue passes off the interval becomes shorter until the normal rhythm is regained. If, however, before this point is reached a new artificial rhythm is induced, the effects are cumulative, the pause at the end of the second stimulation is distinctively longer than that after the first, and successive series of shocks of the same duration and rate are followed by an ever lengthening and deepening period of depression. This offers a difficulty in comparative experiments, because in a heart of low vitality a very considerable time may elapse after a period of stimulation before the normal rhythm has returned completely.

For example, in one experiment the ventricle was beating 51 times per minute spontaneously. Series of rapid shocks were given for 5 seconds

alternately with periods of rest for 10 seconds. The result was increasingly feeble rhythmicity after each series of stimuli. Thus—

after the 1st series the rate during 10 "	was 38 per minute.
.. .. 2nd	36
.. .. 3rd	21
.. .. 4th	18

This cumulative fatigue (Cf. Fig. 7) affects the ventricular pacemaker wherever stimuli are applied. For in one experiment two pairs of electrodes were attached to the heart, one pair at the apex, the other close to the point of section of the bundle: acceleration from stimulation of the apex produced the same fatigue as that from stimulation of the base. The latter was now repeated several times with brief intervals to elicit the cumulative effect. When the pause phase was well elicited the commutator was turned so that stimulation was given at the apex. The subsequent pause was the same as after the immediately preceding stimulation of the base, so that although there had been a considerable interval between the first and second apex stimulations, the intervening base stimulation had induced the same fatigue as if all the stimuli had issued from the apex.

Development of spontaneous rhythm during stimulation.

Fatigue of the rhythmicity persists over the period in which the spontaneous rhythm is developed, and then passes off gradually allowing the previous rate to be regained. The ventricle does not recover during rapid extraneous rhythm but may be further depressed by repeated periods of rapid stimulation. It remained to determine how far the spontaneous rhythm can recover from fatigue if the ventricle is kept active by a slow series of shocks. In some experiments two discs were put on the rotating interruptor, one having three times as many teeth as the other. The shocks passing to the ventricle could be altered in rate from three to one by changing over a commutator which was wired to the two sets of connections on the interruptor and to the primary coil. The interruptor was rotated at the rate which gave on the slower disc the number of shocks desired for the slow phase of stimulation, and the commutator was first set for the faster disc for a definite time to induce fatigue and then changed to the slower disc. When fatigue was elicited by fast stimulation and then shocks rather faster than the spontaneous rhythm were given, the ventricle did not develop spontaneous rhythm during their continuance, but recovery from fatigue occurred, for the pause after the cessation of the slow artificial rhythm was much shorter than if the stimulation had ceased with the quick artificial rhythm. And if the second artificial rhythm was just above the spontaneous rate and continued for some time, there was no pause and almost imperceptible slowing afterwards. The intrinsic rhythm may therefore recover during a series of extraneous stimuli.

provided these are not much more rapid than the spontaneous rhythm, and the longer the slow series continues the shorter the pause after their cessation before a spontaneous contraction occurs.

If the slow shocks were given at a rate just below that of the normal rhythm, the ventricle generally remained without spontaneous rhythm longer than in controls in which the stimulation ceased with the rapid series of shocks, but spontaneous contractions were developed eventually during the continuance of the slow artificial rhythm. In some cases the interval before this occurred was not longer than in the controls in which the stimulation ceased with the rapid fatiguing shocks, the slow stimulation apparently not retarding recuperation in these. The first spontaneous contraction was distinguishable from the artificial ones preceding it only by its occurring slightly in advance of the stimulus, and the electric shock falling during its refractory phase had no effect (Fig. 8). The second and third were also

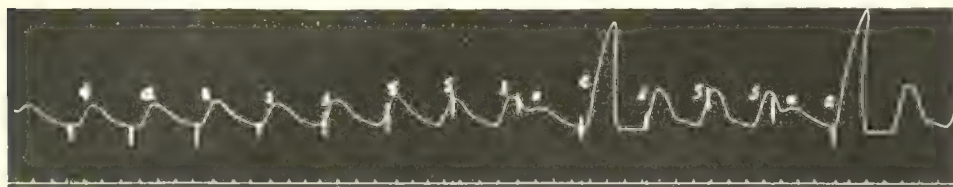


Fig. 8. Cat's heart prepared as described. Rate of spontaneous ventricular beat 107. Stimulated artificially at the rate of 250 per minute for 10 seconds. Then at 84 per minute. The figure gives the tracing 6 seconds after the commencement of this slow stimulation. The time of each stimulus is indicated by a line drawn across the tracing. The contractions marked *a* are due to these artificial stimuli, while those marked *s* are spontaneous. Some doubt may be entertained as to whether the first contraction marked *s* is really spontaneous, and also in regard to the large contractions marked *a* after the extrasystoles.

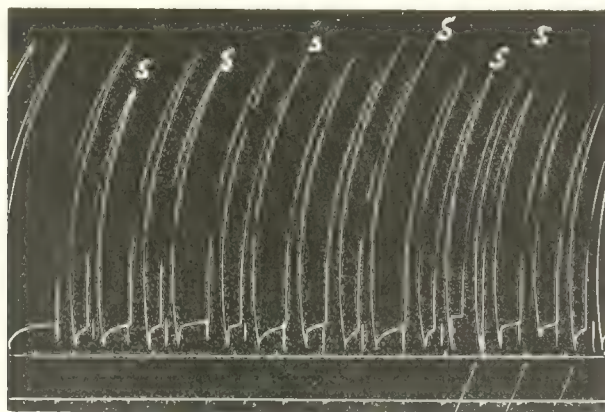


Fig. 9. Development of spontaneous rhythm during artificial stimulation. Original rhythm 80 per minute. Artificial shocks 190 per minute for 15 seconds. Then shocks at 53 per minute continued. No spontaneous contraction for 15 seconds. One contact failed just as Fig. 9 began. The spontaneous contractions are marked 'S'. Time in seconds. Lowest line indicates the rate of stimulation.

correspondingly premature and similarly the electric shock was fruitless. As the interval between the spontaneous beat and the shock increased, however, the latter fell later in the contraction phase and finally reached the ventricle during the reactive phase and caused an extrasystole. The procedure then repeated itself, the spontaneous rhythm being interrupted every third, fourth or fifth beat by an extrasystole arising from the electrical stimulus.

Occasionally, as in Fig. 9, a more or less regular alternation of spontaneous and artificial beats was met before the spontaneous rhythm gained the upper hand.

These experiments indicate that the spontaneous rhythm may be retarded but is not entirely suppressed by a series of artificial stimuli, provided that these are given at a slower rhythm than the spontaneous ventricular rate; during the continuance of the slow artificial rhythm, the spontaneous energy may accumulate until it gives rise to a contraction. The last mentioned experiment, Fig. 9, is of especial interest, because here the spontaneous rhythm arose and continued during the artificial, so that the ventricle was subjected to two sets of impulses simultaneously, one the artificial, the other spontaneous. And in part of the tracing the spontaneous contractions alternate with those arising from the artificial shock. Here the spontaneous contraction begins before the regular shock is given, and the latter falling during the refractory phase of the spontaneous cycle fails of effect. There is then a pause until the next artificial shock arrives when a new contraction occurs to be followed again by a spontaneous contraction. The pulse period of the beat aroused by the shock was considerably shorter than that of the spontaneous contraction; in other words the spontaneous contraction was followed by a pause during which a second spontaneous beat might have occurred without interference from the electric shock.

If the impulses from without reached the ventricle from the auricle instead of the electric coil, the same form of tracing would have been obtained, but the beats which I have called spontaneous would then have been ventricular extrasystoles, and the first six contractions would have been *pulsus bigeminus*. The similarity is so marked that there was a temptation to suggest that the clinical bigeminal pulse arises from the development of a ventricular rhythm along with the normal rhythm of the heart; the ventricular extrasystoles would then arise from the rhythmical formation of an impulse in the ventricle, independently of the impulse developed in the pacemaker of the heart. This explanation of the bigeminus is surrounded with difficulties, however, and until these have been considered, it would be premature to abandon the view that the extrasystole of the bigeminus pulse is in some way the result of the previous contraction. This view is in fact supported by the further course of this experiment, for when the artificial shocks were stopped a distinct pause occurred, lasting longer than the interval between the spontaneous contractions previously, which suggests that these were in some way dependent on the artificial rhythm.

Occasionally in ventricles which were perfectly regular before and during the stimulation, the first or second contraction during recovery was followed by a very rapid secondary contraction (or extrasystole) (Fig. 10), or each of the first few beats was succeeded by this secondary movement. As the rhythm accelerated to its normal rate, however, these disappeared. Here, I suppose, rhythm had developed at two different points in the ventricle during the pause and a stimulus was formed at each, one giving rise to the

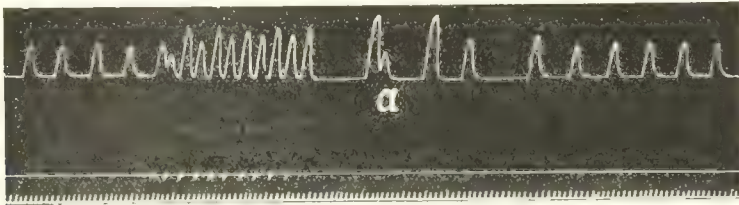


Fig. 10. Cat's heart. Spontaneous ventricular rate was regular. At *a* a secondary contraction (extrasystole) after the first point took place at recovery.



Fig. 11. Cat's ventricle. Spontaneous extrasystole followed by powerful contraction without any prolongation of the intervening pause. The next two contractions are also unusually powerful.

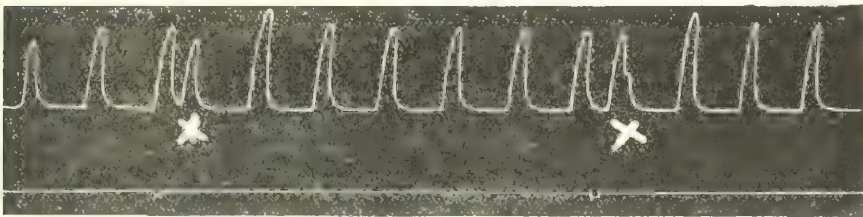


Fig. 12. Cat's ventricle. Two extrasystoles from electric shocks. Each leads to a distinct strengthening of the following two systoles.

large beat, the second to the extrasystole. The process may be repeated if the dominant point only slowly recovers from its fatigue, but as soon as it reaches a fair rate its activity has the same repressing effect on the other rhythmogenic points as the rapid artificial stimuli exercised upon itself previously. In some stimulations the ventricle passed into fibrillation, and recovery from this was followed by a very long pause before the spontaneous rhythm set in.

As regards the contraction power of the heart in these experiments, the stimulation very often gave rise to the staircase phenomenon. The first spontaneous contraction afterwards was also powerful, sometimes larger than those during the rapid rhythm, sometimes of equal size. The following contractions became smaller as the spontaneous rhythm was further developed and the interval between the beats became shorter. In the state of the heart which exhibited the long pauses after acceleration, which I have interpreted as fatigue of the rhythmicity, the contractility was not only not fatigued but actually increased, as was shown by the staircase phenomenon. After an extrasystole the large "post-compensatory" contraction is well known and has generally been regarded as the result of the preceding "compensatory" pause. Rihl⁷ however points out that it may occur without a compensatory pause, for example, after an interpolated beat in which the pulse interval is actually much shortened. I have occasionally seen this also, and in one case not only the first beat after the interpolated extrasystole was higher than normal, but the two following ones (Fig. 11 and 12). The extrasystole was in fact the first of a staircase, the next was its apex, and in the following beats there was a slow return to the normal contractility. It may be questioned, however, whether this strengthening effect of an extrasystole plays a part in more normal hearts, in which the staircase phenomenon is less easily elicited. And in these the power of the post-compensatory contraction probably owes more to the length of the preceding pause than to the directly favourable effect of the extrasystole. On the other hand there can be no question after Rihl's work that in certain hypotonic conditions of the heart an extrasystole in itself increases the power of the succeeding spontaneous contraction. It may be recalled that Rihl's observations were made on hearts which were cooled in order to slow the rhythm and this renders the contraction abnormal and favours the appearance of the staircase phenomenon. This supports the view stated above that the strengthening effect of an extrasystole on the following contraction is of the same nature as the staircase phenomenon.

In auricular fibrillation both in man and animals, one of the characteristic changes in the pulse is the variation in the strength of the beat, which often bears no relation to the length of the preceding interval. This may perhaps arise from an abnormal contractility comparable to that seen in the animal heart when exposed to cold and the other disadvantageous conditions mentioned already. For while in these experiments the heart is beating at a normal rate and any prolongation of the rest phase is followed by a contraction of unusual strength, a sudden acceleration may also increase the strength of the following contractions which assume the well-known staircase form. In Fig. 3 for example the third artificial stimulus leads to a very powerful systole although the rest phase preceding it is very much shorter than that preceding any of the spontaneous beats. Yet in the same figure the first spontaneous contraction after the artificial stimulation is still more powerful, though the pause preceding it is very much longer than

that of the spontaneous contractions and of the contractions during stimulation. In this condition of the heart the prolongation of the pause of rest strengthens the contraction, but acceleration and corresponding shortening of the rest phase also increases the power of the systole. The variation in the strength of the beats in auricular fibrillation may be due to a similar mixture of factors, the one strengthening the contraction according to the length of the preceding rest phase, the other strengthening it in spite of the shortened rest phase through the factor which lies at the base of the staircase phenomenon.

It is worthy of note that the staircase phenomenon may be presented by hearts which exhibit alternation of contractions at the same time (see Fig. 3).

In three experiments the effects of helleborein were tested on the fatigue of the spontaneous rhythm. The contractions were increased in strength, and after the drug had acted for some time the rate was considerably accelerated. But even before this second effect was developed, helleborein had a distinct action in lessening the fatigue from artificial stimulation. The pause after the acceleration became shorter and disappeared completely in two experiments before the intrinsic rhythm was noticeably quickened. There seems therefore reason to suppose that the members of the digitalis series would lessen the tendency to the Stokes-Adam syndrome in complete block, as indeed has been shown by Bachman.¹

SUMMARY.

In these experiments the mammalian heart was perfused, the auriculo-ventricular bundle divided, and the behaviour of the ventricle examined during spontaneous rhythm and under electrical stimulation.

Acceleration of the rhythm, spontaneous or artificial, is followed by a period of slow contractions with pauses, which gradually give place to the usual idio-ventricular rhythm.

This slow phase is not inhibitory in origin, and the contractility and excitability of the ventricle are not diminished. The phenomenon is due to a depression of the function of stimulus formation in the ventricular pacemaker which presents analogy to the fatigue of striated muscle. The extent of this depression depends on the rate and duration of the previous acceleration.

It is suggested that in the intact heart the ventricular pacemaker is kept in a state of fatigue by the impulses reaching it from the Keith-Flack node, and that when these are excluded from it by section of His' bundle, the slow development of the idio-ventricular rhythm is due to the ventricle recovering only gradually from this fatigue. And that in cases of complete block in man the phases of extreme slowing arise from previous acceleration having exhausted the ventricular pacemaker in a ventricle already reduced by disordered nutrition.

The conductivity of the heart is also susceptible to fatigue and is normally in a condition of submaximal activity. The contractility and excitability by electric shocks are not diminished by prolonged and excessive activity.

The partial fatigue of the functions of stimulus formation and conductivity does not preclude altogether the performance of these functions, but retards them. Fatigue of the rhythmicity slowly disappears even during the activity of the ventricle provided this activity is limited in extent. On the other hand artificial acceleration repeated several times progressively augments the fatigue of the ventricular pacemaker.

The state of the ventricular nutrition which favours the fatigue of the rhythmicity also leads to an increased pause after a single premature contraction. It does not appear to be identical with the hypotonic condition in which *pulsus alternans* occurs. The same fundamental change in the nutrition may lie at the basis of the staircase phenomenon.

The expenses of this investigation were defrayed by a grant from the British Medical Association.

NOTE.—While this paper was passing through the press, Hering discussed (Pflüger's Archiv. f. d. ges. Phys. 1911, CXLIII, 370) the considerable amount of evidence already published that the spontaneous stimulus formation is independent of the excitability of the heart muscle and concluded as I have done, that these two functions may vary independently. He further raised the question whether the electrical excitability can in all cases be regarded as a measure of the natural excitability of the heart muscle.

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OBSERVATIONS UPON DISORDERS OF THE HEART'S ACTION.

BY THOMAS LEWIS.*

(Cardiographic Department, University College Hospital Medical School.)

During the course of a systematic investigation of the heart by means of graphic methods, I have made a number of observations which are not immediately connected with each other. It is my desire, at the present time, to place certain of these observations upon record, and I shall proceed to do so, under distinct headings.

PART I. A SERIES OF CLINICAL CASES.

Section 1. An observation upon ectopic impulse formation.

For the past eighteen months, a lad of eighteen years has been repeatedly examined by means of the electrocardiographic method, because he presented at the first examination, and has continued to show, a hitherto undescribed disorder of the heart's mechanism. He is an engineer's labourer and has always enjoyed excellent health, having suffered from no infectious disease and having been perfectly free from all symptoms of heart affection. The irregularity of his heart's action was discovered during a routine examination by Dr. Marris, to whom he went for the treatment of a bilious attack which resulted from a dietetic indiscretion. The dimensions of the heart are hardly abnormal. The percussion limits lie 1 and 4 inches to the right and left of the mid-sternal line respectively. The sounds are natural. The irregularity has been present constantly from the time when it was first observed until the present day, and its nature, in so far as I shall consider it at the present time, has been unchanging. It consists of disturbances of the sequence which result from the frequent occurrence of premature contractions, and these early contractions arise, as shown by repeated examination, from a fixed and ectopic auricular focus. An example of the irregularity is shown in Fig. 8 (an electrocardiogram from lead II). The ventricular complexes of rhythmic and premature heart beats have a constant and normal form, the auricular complex of the premature beat is inverted. The electrocardiogram shown in this figure is not exceptional, it is an example of the

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pictures, now well-known, which are found when premature auricular contractions are present. The new fact is illustrated in the next figure (Fig. 9), in which electrocardiograms, taken separately from leads *I*, *II* and *III*, are shown. The picture from lead *II* of this figure may be compared with Fig. 1. A premature beat of the usual form is seen towards the end of the curve (Fig. 9 *II*), but in contrast to Fig. 1, the beat which follows it is abnormal.* It springs from the same focus as does the premature beat, a fact which is evidenced by the similarity of the electric changes. Precisely the same phenomenon is seen in the two other leads (leads *I* and *III*) of the same figure. In lead *I* the auricular representative is almost iso-electric, both in the premature beat and in that which follows it. In lead *III* it is inverted in both beats.

What is the nature of the second abnormal beat? Is it of precisely the same nature as the premature beat which it follows: or is it comparable to the beats of the normal type? The answers to these questions are perhaps uncertain, but the evidence is chiefly in favour of the second view. That it belongs to the same order of pathological or *heterogenetic* contractions, as I have termed them, to which premature beats belong, is improbable. When a pair of premature beats occur, they follow each other closely, and I have curves from the same patient in which there is but a very short gap between the separate beats of such a couple. In the present figures, the pause between them is always long. On no occasion have pauses of intermediate length been seen: the pause is generally equal to or falls only slightly short of that which follows an isolated abnormal contraction, and is usually larger than the pauses separating beats of the regular rhythm in the same patient.† It is consequently probable that the second abnormal contraction has arisen by processes similar to those which create the normal beats; processes which are physiological or *homogenetic*.

The occasional slight prematurity of the second ectopic beat, and its site of origin, may be explained by supposing that the discharge of the first or true premature beat hastens physiological impulse formation at the focus in which it arises, and that the new focus, stimulated in the manner suggested, wins in its race with the pacemaker to produce the next physiological impulse. Such a view is supported by other observations. On several occasions I have observed that if the auricle of an animal is stimulated by means of an interrupted current so that a regular tachycardia, or succession of responses, is produced at a faster rate than that of the normal rhythm, the first beat of the escaping auricle, when stimulation ceases, comes, not from the pacemaker, but from the point originally stimulated.

* The occurrence of the abnormal beat has been as common as that of the normal beat, and both have been extremely frequent.

† The analysis is complicated by the occurrence of the slow but accelerating heart rate which succeeds each interruption.

Section 2. An instance of premature auricular contractions, followed by pauses considerably shorter than those separating the regular heart-beats in the same case.

A man of 64 years, who gave a history of rheumatic fever at the age of 24, and who has physical signs of extensive fibroid change in the left lung, was sent to me because he had an irregular heart action.

Apart from the irregularity, there were but few physical signs. The limits of the heart's dulness were normal, and there were no symptoms which could be directly referred to the heart. A systolic murmur at the apex was alone detected.

Several strips of curve, taken from the radial artery, are shown in Fig. 1. Premature beats occur from time to time in the curves. In no instance is the pause following a premature beat compensatory: in most instances it not only fails to be compensatory, but it is considerably shorter than the pause separating the beats of the regular rhythm, which comes before and after the disturbance.

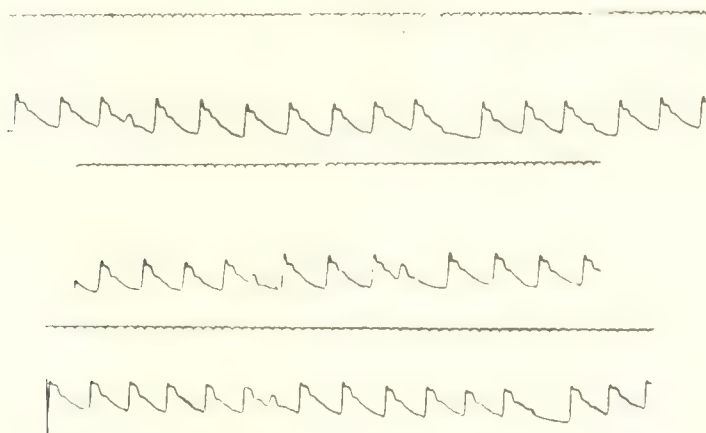


Fig. 1. Radial pulse curves from a patient who showed premature auricular contractions. The pause following a premature beat is usually considerably shorter than the pause separating rhythmic beats. The time marker is in one fifth seconds in this and all polygraphic curves.

The corresponding electrocardiograms, taken at the same time, are shown in Fig. 10*a* and *b*. Satisfactory curves were obtained from lead *II* only: those from leads *I* and *III* being too tremulous to be of value. Altogether, three premature beats are seen. All arise in the auricle; and, judging from this lead alone, they arise in close proximity to the pacemaker, for the auricular complexes, corresponding to rhythmic and premature beats, seem identical in outline. One of the premature beats is followed by a long pause, but the two remaining ones are succeeded by pauses, which are shorter than the pauses separating rhythmic beats.

It is known that electrical excitation of the auricle, in the neighbourhood of the great veins, produces premature beats which are followed by short pauses; but pauses which are shorter than those separating rhythmic beats have not been seen previously. Presumably they are due to the presence of a somewhat rare phenomenon, namely, stimulation of physiological impulse formation at the point at which they arise, so that the succeeding physiological impulse is formed more rapidly than usual.

Section 3. In a patient who presented a paroxysm of regular tachycardia, auricular fibrillation developed, and quick changes from one condition to the other were recorded. The same patient demonstrated a regular and exceptionally rapid action of the ventricle while the auricle continued to fibrillate. Curves were obtained within 24 hours of death.

The patient, an unmarried girl of 17 years, was admitted to University College Hospital on November the 9th, 1911, and presented evident symptoms and signs of heart failure.

Her heart was said to have been affected for 7 years: at the age of 10 she lay in a bed at Gt. Ormond Street Hospital, suffering from swelling and pain of the joints. Her symptoms, shortness of breath, palpitation, weakness, cough and sleeplessness had been conspicuous for 11 weeks prior to her admission.

Cyanosis, orthopnoea and a slight degree of conjunctival jaundice were noted at her entrance into hospital. Ascites, some œdema of the legs, fullness of the veins and enlargement of the liver were present. Crepitations were audible at the bases of both lungs.

The heart's impulse was visible in the third to sixth interspaces; the limits of dulness lay 1 and 6 inches to right and left of the mid-sternal line as she lay in bed. Systolic and diastolic thrills were present at the apex, and at the same point corresponding murmurs, the last of a grinding character, were audible. The first sound was accentuated, and seemed to fill the whole of diastole; the ventricular rate was 168 per minute, the heart's action being perfectly regular.

The patient was placed upon digitals on the 9th; it was administered in doses equivalent to a drachm and a half of the tincture a day. On the 10th this dose was reduced to an equivalent of 40 minims a day and this was continued until the 17th. She vomited on the last two days of its administration.

I saw her on the 12th, when her pulse was stated to have first become irregular. When examined, a regular tachycardia was found, which was uninfluenced by posture and the rate of which was 153 to 155, but in a few minutes the heart became irregular for a brief period, returning to its former state. This was repeated very many times and the action

of the heart is illustrated by Fig. 2 and 3. In Fig. 2 a period of regular tachycardia, accompanied by the ventricular form of venous pulse, passes into an irregular period also accompanied by the ventricular form of venous pulse. In Fig. 3, a short irregular period is interposed between two regular

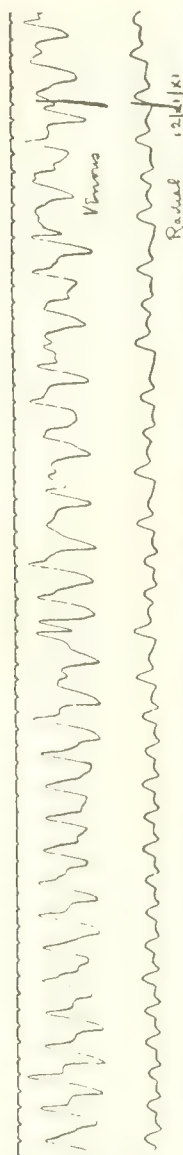


Fig. 2. A polygraphic curve showing the passage of a period of regular tachycardia into an irregular tachycardia. The venous pulse is of the ventricular form throughout. Where a long pause occurs, prominent stasis waves are also present. The mechanism in Fig. 2 and 3 is of the same nature; the figures show the passage of regular tachycardia of auricular origin into auricular fibrillation. The electrocardiogram corresponding to the regular period is shown in Fig. 11.

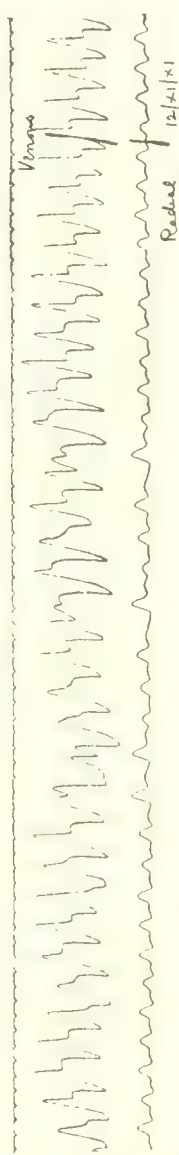


Fig. 3. A polygraphic curve which opens with a paroxysm of regular tachycardia, the rate of which is approximately 150 per minute. The venous curve is of the ventricular form. The regular paroxysm ends and gives place to a period of irregularity of about 5 seconds duration. Then the regular tachycardia is resumed. The period of irregular tachycardia is also accompanied by the ventricular form of venous pulse.

periods. The change from one action to the other continued at short intervals for an hour, and there is little reason to doubt from these curves and subsequent observations that the changes were from regular paroxysms

arising in the auricle to auricular fibrillation. Directly after the polygraphic curves had been secured, the patient was examined electrocardiographically, but by this time a regular paroxysm had become continuous. The curves are shown in Fig. 11. The heart rate is 156 per minute. In lead *I*, *R* is small, *S* is large. In lead *III*, *R* is exaggerated; these are signs which are found almost constantly when the right ventricle is hypertrophied and mitral stenosis is present. The auricular representative is seen in each lead, and it appears to fall a little before the termination of the preceding systole of the ventricle: it is not of the form which usually accompanies mitral stenosis, and arguing from this fact and from the general character of the paroxysm, I am led to the conclusion that the paroxysm was of ectopic auricular origin.

On the 17th the pulse became slow, regular and palpably dicrotic. A mid-diastolic murmur was present: the ventricular form of venous pulse was maintained. The condition of the patient had improved remarkably: the cyanosis, dropsy and orthopnoea had vanished, engorgement was less, the liver was barely palpable: a little ascites remained. Improvement continued, the pulse remaining regular at a rate of 80 beats per minute. On the 18th the digitalis was continued in small doses: 9 minims a day were given until the end. On the 18th and until the 23rd the pulse was regular, the rate varying between 80 and 90. Electrocardiographic curves taken on the 22nd showed a perfectly regular ventricular action at a rate of 90 per minute. They are shown in Fig. 12. The ventricular complexes are of similar general form to those of Fig. 11, though the excursions of the string have decreased and *T* is no longer completely inverted in leads *II* and *III*. There is no sign of co-ordinate auricular contraction, but *P* is replaced by the characteristic oscillations of a fibrillating auricle. That the oscillations arose in the auricle is evident from the special leads taken to demonstrate it. Fig. 13 shows three of these leads: electrodes were placed over the right auricle (*I*), the lead showed conspicuous oscillations: leads were taken from the outer end of the third left interspace to the apex (*II*), and from the epigastrium to the apex (*III*); in these two leads only very faint traces of oscillations were detected from time to time. On the 22nd, therefore, the auricles of this patient were fibrillating while the ventricles maintained their regularity at a rate of 90 beats per minute. Now when auricular fibrillation is accompanied by a regular ventricular action it is assumed that no impulses reach the ventricle from the auricle. The ventricle is considered to respond to impulses formed in the junctional tissues, the intrinsic ventricular pacemaker. Such is the assumption in the present case, though the ventricular rate of 90 must be considered quite exceptional: the ventricular rhythm was quite uninfluenced by posture and deep respiration. A similar instance, in which the rate of the ventricle was 70, has been spoken of by Mackenzie,¹⁰ a case which I examined electrocardiographically. The findings were the same as those stated for the present patient, with the exception that the ventricular rate was slower. It should be remembered that complete dissociation has been seen in an adult in whom the auricles beat at

138 and the ventricles at 66 per minute.¹⁵ While the intrinsic ventricular rhythm is usually 30 or thereabouts, it may be much faster in these exceptional cases: it is especially fast when heart-block has been induced by the administration of digitalis. The complete obstruction of auricular impulses, which has to be assumed in the present case, is attributed to the digitalis: the patient was under its full influence when the regular pulse appeared. The block continued until the 23rd, at which time the patient was on 9 minims a day on digitalis tincture and had not taken the heavier doses for five days.

On the 24th the pulse was grossly irregular and electrocardiograms gave the characteristic pictures of auricular fibrillation (Fig. 14), the ventricle responding to the fibrillation impulses. The ventricular rate was approximately 84 per minute. A number of the ventricular beats were premature (marked with an asterisk in Fig. 14) and of ventricular origin: the remainder showed conspicuous variation in the amplitude of *R*; *T* was inverted in leads *II* and *III*. During the evening of the same day the patient was comfortable and seemed to continue her improvement. She slept well during the following night and was sleeping, though a little restless, a quarter of an hour before death occurred. At this time the pulse was still irregular, as on the preceding day. Apparently she died in her sleep. The patient in the next bed called the nurse, saying that her neighbour looked pale and that her head was back. The girl was dead.

The case may be summarised in the statements that in a case of mitral stenosis admitted for heart failure, regular paroxysms of tachycardia arising in the auricle alternated with periods of fibrillation, while the patient was under digitalis; that subsequently, while the auricles remained in a state of fibrillation, the ventricles beat regularly at 90 per minute: that the regular action of the ventricle gave place to an irregular action, in which *R* showed conspicuous variation in height, in which *T* was inverted in leads *II* and *III*, and in which premature ventricular beats were scattered: the patient died unexpectedly while the heart continued to beat in this manner.*

Section 4. An account of a patient who came under observation with a heart rate of 150. The auricles were found to be beating at 300 per minute. Upon digitalis the auricle passed into fibrillation and subsequently the normal heart rhythm was resumed. A further and brief account of three similar cases.

W. G., a French polisher, 60 years of age, was admitted to University College Hospital on November the 19th, 1911, complaining of shortness of breath, cough and dropsy. He gave a history of having had periodic attacks

* Instances of unexpected death in heart disease are common and of extreme importance. In a number of patients, upon whom graphic observations have been made and who have died without warning, premature ventricular contractions, with or without auricular fibrillation, have been present. The suggested cause of death is sudden cessation of the circulation as a result of the onset of ventricular fibrillation.

of breathlessness of a distressing and exhausting character for three and a half months. He had a very severe attack in October, 1911, which lasted three days. Previously his health had been good: at 17 he was infected with gonorrhœa: at 23 he was laid up for three weeks with a chest ailment of which he remembers but little. He had had neither rheumatism nor syphilis. Of alcohol he had drunk temperately: he had been a moderate smoker.

Upon his admission the temperature was 98° Fahr., the patient was orthopnœic and slightly cyanosed: there was a little dropsy in the legs: signs of fluid in the abdomen were present. The diffuse heart apex beat lay in the fifth and sixth interspaces. The right limit of dulness was $1\frac{1}{4}$, and the left 6 inches, from the mid-sternal line. The sounds at the aortic cartilage were normal: at the pulmonary cartilage the second sound was accentuated: at the apex the first sound was accentuated. A systolic murmur was present at the apex. The pulse rate was 150 and did not alter with posture. There seemed to be no arterial thickening: the systolic blood pressure varied from 116 to 120 mm. Hg.. The liver was enlarged. The urine was normal. The subsequent events are related in the ensuing paragraphs.

On November the 25th he was placed upon the fresh infusion of digitalis, three drachms being given four times a day.

On the 26th electrocardiograms were taken: as subsequent events proved, they showed 2:1 heart-block, the auricular rate being 293 per minute (Fig. 15). From the time of his admission the pulse rate had continued persistently at 145-150 per minute, and the presumption is that during the whole of this period 2:1 block was present. Occasional premature ventricular contractions (*P.B.*) were seen and disturbed an otherwise perfectly regular heart action.

On the 28th the mechanism remained unchanged. The auricular rate, recorded electrocardiographically on this day, was 300 per minute.

On December the 1st the recorded rate of the auricle was 299, the ventricle beating at half this rate and occasionally becoming slower as a result of the presence of 4:1 periods (Fig. 16).

On the 2nd the recorded auricular rate was 288: the ventricle beat at 72, except for short periods of the 2:1 ratio.

On the 3rd, 4:1 block was established, the rate of the auricle being 292.

On the 4th, the 4:1 block was maintained, the auricular rate being 288. (Fig. 17). The heart limits were $1\frac{3}{4}$ and 6 inches on either side of the mid-line. Systolic and faint early diastolic murmurs were audible at the apex. The auricular sounds could not be heard. The whole condition of the patient had improved conspicuously: there were no symptoms, the cyanosis, dropsy and liver enlargement had disappeared. Pressure upon the right or left carotid sheath, even when light, produced an almost invariable cessation of ventricular action for several seconds (see Fig. 4, 5 and 18). Cessation of the pulse for six seconds was accompanied by pallor and faintness: though consciousness was never lost. During the whole of the period of

ventricular systole the auricles continued their rapid action as before. On this day the chest was screened but the movements of the auricles were not apparent.

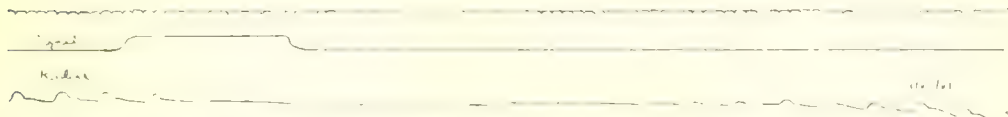


Fig. 4. A radial curve and signal showing the effects of light compression of the right vagus. The vagal compression lasts for a little more than three seconds. Within a second of its onset the pulse disappears and no beat is recorded for a period of approximately 7 seconds. The first radial beat following the pause is weak, and the succeeding beats, which are regularly spaced, show the staircase phenomenon.

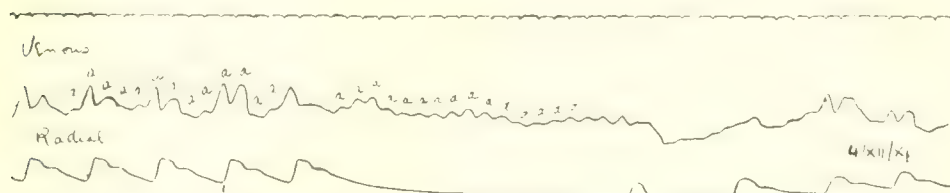


Fig. 5. Venous and radial curves from the same case, showing the effect of left vagal compression. During the opening phase of the curve, 4:1 heart-block is present. The venous curve during this period consists entirely of *a* waves, though it has a superficial resemblance to a normal venous curve, with *a*, *c* and *v* waves occurring as accompaniments of each ventricular heart cycle. When vagal compression produces a higher grade of heart-block, the separate *a* waves become perfectly distinct.

On December the 11th the pulse rate suddenly fell from 72 to 44 and the action of the heart became grossly irregular. Electrocardiograms showed that fibrillation had set in (Fig. 20). The symptomatology was otherwise unaltered.

On the 12th the digitalis was stopped. On the 13th, 14th and 18th polygraphic records showed gross irregularities of the pulse and rates of 45, 56 and 53 respectively.

On the 20th, fibrillation was still present, but the ventricular rate had risen to 62.

A period now intervened during which no observations were made. Upon the 4th of January the heart action was normal and the rate of auricle and ventricle was 63. Electrocardiograms of the restored action, but in which the rate is 90, are shown in Fig. 21; they were taken on the 6th. On both dates premature auricular contraction interrupted the otherwise regular rhythm.

The patient was discharged, much improved in health, on January the 8th.

On the 20th the normal rhythm was still present, interrupted as before by single and successive premature contractions, some generated in the auricle, others in the ventricle. Pressure upon the carotid sheath on this day had

absolutely no effect, whereas on the previous occasion, when the patient was under the influence of digitalis, the carotid pulsation could be scarcely felt without producing conspicuous slowing of the pulse.*

Description of electrocardiograms. The figures which are published in illustration of this case may be described most conveniently without reference to their chronological order.

Fig. 21 was taken after the resumption of the normal rhythm. The photograph consists of one strip of curve from each lead, and each strip contains a solitary premature contraction, springing from the auricle. In lead *I*, the auricular contractions of the normal cycle are represented by two small pointed summits (marked *x x* in the figure). The auricular contraction of the premature cycle is represented by a single pointed summit (marked *P* below the line). In leads *II* and *III*, also, the premature auricular summits differ in outline from those of the normal cycle. Fig. 21 consequently shows a normal rhythm, interrupted by premature auricular contractions which arise in an ectopic focus.

The interpretation of Fig. 20 is equally clear. Comparing the curves with the series in which normal cycles are present, it is evident that co-ordinate contraction of the auricle is in abeyance, for there is no sign of the presystolic *P* summits of Fig. 21. On the other hand, the ventricular action is slow and extremely irregular: prominent oscillations characteristic of a fibrillating auricle are present.

Fig. 17 shows the curves obtained from the three leads while the heart was beating regularly, and while 4 : 1 heart-block was present. The outlines of all the auricular waves may be clearly distinguished in leads *II* and *III*. In lead *I*, the outline of two *P* summits are easily recognised in each pause, the remaining *P* summits, of which there are two to each cycle, fall with *R* and *T* respectively. The auricular summit has the same form as has that of the premature beat in Fig. 21 *I*. The *P* representative of leads *II* and *III* form a continuous series, so that the string is never at rest. The activity of the auricle appears to be continual; the rest between the beats is absent or inappreciable in duration. The relation of the *P* summits, in leads *II* and *III*, to the deflection of the string produced by ventricular systole, are seen to advantage in Fig. 19. The curve was taken with the string standardised to give a deflection of $1\frac{1}{2}$ cm. to the millivolt, and at a faster speed than that at which the remainder of the curves were taken. The continuity of the auricular representatives is broken by the ventricular deflections, but for one cycle in each of these curves, the auricular portion of the electrocardiogram has been reconstructed, by drawing upon the original curve, so as to make the relation of the auricular and ventricular portions of it evident. The unvarying, regular and rapid beating of the auricle, displayed in this fashion, is also exposed in Fig. 18, taken on the same

* The patient returned with a new paroxysm on February the 24th, 1912. It was of the type seen in Fig. 15.

day. The right carotid sheath and the contained vagus were pressed upon, at or about the time at which the curve commences. Two ventricular cycles, belonging to a period of regular 4 : 1 heart-block are shown : the ventricle ceases to beat for 18 auricular cycles under the influence of the stimulation of the vagus ; following upon the release of compression the preceding mechanism, *i.e.*, 4 : 1 heart-block, is rapidly restored.

A few days before Fig. 17 was secured, that which is shown in Fig. 16 was obtained. A comparison of the two figures renders detailed description unnecessary : it is evident that a varying degree of heart-block is exhibited, while the auricular rate is continuously rapid. Periods of 2 : 1 and 4 : 1 heart-block are mixed together.

It is from a careful consideration of the curves, which have been described, that the interpretation of Fig. 15 becomes clear. The beating of the ventricle is approximately at 146 beats per minute : in Fig. 17, the ventricular action is but about half this rate. It is Fig. 17, and the transition curve (Fig. 16), which suggests so strongly that the rapid auricular action is continued throughout the whole series (namely, Fig. 15, 16 and 17). Fig. 15 is important because it shows the picture presented by the patient when first seen. A correct interpretation of this isolated curve would be difficult or impossible. Yet with the full series of curves in view, it is a matter of no great difficulty. The little *P* summits, two to each ventricular contraction are clearly distinguishable in lead *I*. In Fig 19, leads *II* and *III*, the auricular activity is represented by a continuous wavy line. The same form of electric disturbance may be followed throughout leads *II* and *III* of Fig. 15, though in this instance it is broken more frequently by ventricular deflections.

Additional cases of rapid auricular action. The interpretation of this series of curves has thrown considerable light upon a number of isolated curves in my collection. One of them has been published recently by Dr. Mackenzie in this journal,¹¹ but its interpretation was not possible at that time. With his permission, I republish it as Fig. 23 of the present communication and am now able to place the companion curve, namely, that showing the normal heart action in the same case, side by side with it (Fig. 22). The small and upright *P* summits of lead *I* (Fig. 23) are quite evident and are regularly spaced ; the deep inverted deflections of leads *II* and *III* are also evenly spaced and are now equally evident. The rate of the auricular contractions in this curve is approximately 320 per minute. The patient, as the original account of him tells, was the subject of paroxysms of tachycardia of two forms. In one the pulse beat at 140-150 per minute, in the other the pulse was observed to mount to rates of 280 and 300 per minute. The explanation of these rates is now apparent : during the slower paroxysm, 2 : 1 heart-block was present ; during the faster paroxysm it vanished.

Two other patients, from whom I have obtained electrocardiograms, during attacks of tachycardia, have shown similar phenomena. The curves

of these two patients are so much alike that a single illustration will suffice for both.

Electrocardiograms are shown in Fig. 24, in which auricular contractions are clearly represented in all leads, the *P* deflections occur twice as frequently as do those of the ventricle. The rate of auricular contractions is 313 per minute, while that of the ventricle is 156.5 per minute. The curves were taken from a patient in whom the rate is said to have been maintained* for a period of three years. Under a full course of digitalis, the fast and regular auricular action has since given place, first to fibrillation, and later to the normal rhythm.

In the fourth case, which I have personally examined, the rate of auricle and ventricle were 260 and 130 respectively.†

Discussion. Several instances of very rapid and regular action of the auricle have been recently placed on record. Notable examples of the phenomenon are Hertz and Goodhart's case;³ that more recently described by Jolly and Ritchie,⁵ and the three cases described by Rihl;¹² in these five patients the highest recorded rates of auricular contraction were 236, 300, 315, 222 and 214, respectively. In all these cases heart-block was also present at some period of the observations, so that the ventricular rate was but a fraction of the auricular. To these records I am able to add Mackenzie's case¹¹ and a new series of three cases; it will be evident that the condition is not so rare as might have been supposed, and it becomes clear that many of the older accounts, which state that paroxysms of tachycardia may be accompanied by ventricular rates of from 200 to 300 per minute, are no longer open to the scepticism with which they have hitherto been regarded, in the absence of graphic records. The sudden and exact doubling of already accelerated ventricular action, such as has been described by Hoffmann,⁴ also receives a ready explanation. The "Auricular flutter" as Jolly and Ritchie have named it, is commonly associated with heart-block, the degree of which may vary, producing halved ventricular rate from time to time.

The recognition of a type of paroxysmal tachycardia in which extreme rates of auricular contraction are maintained, is of considerable importance, for such patients are ever on the verge of developing auricular fibrillation; and, as Mackenzie has pointed out, the production of fibrillation may be beneficial; not only is the heart rate reduced at its onset, but by the abolition of the accelerated and regular action of the auricle, the restoration of the normal rhythm may be hastened. Of the three cases which I have added to the published series, two have reacted at the administration of digitalis, and the auricle has passed into fibrillation. In both of these the normal rhythm was restored soon after the administration of the drug ceased. The third case passed from observation before the action of the drug could be

* For this information and that which follows I am indebted to Dr. Blackburn of West Hartlepool.

† Three additional cases have since been observed. The rates of auricle and ventricle were 320 and 160, 224 and 112, 334 and 167, respectively.

tested. In Mackenzie's case fibrillation was produced by digitalis and the normal rhythm was subsequently restored. The auricle also passed into fibrillation in one of Rihl's cases.

A brief description of the polygraphic curves, which these patients yield during periods of auricular acceleration, is desirable. In some the records are clear, as in the patients of Hertz and Goodhart, and those of Jolly and Ritchie; much more frequently they are obscure. In the four cases which I have seen personally, and in an additional case from which I have seen the polygraphic tracings alone, the venous records were anything but easy to read. The auricular summits are often small and inconspicuous, and many of the curves have waves which might readily be misinterpreted as *a*, *c* and *v*, three such waves commonly occurring with each ventricular cycle. An example is shown in Fig. 6, a curve taken from the case which has

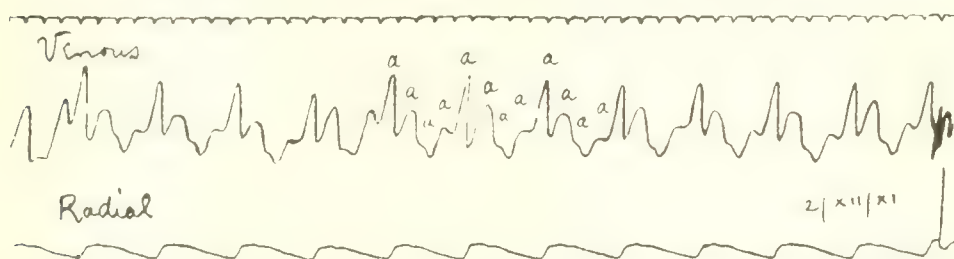


Fig. 6. A polygraphic curve during a period of 4:1 heart block. The venous curve consists entirely of *a* waves; though, in the absence of electrocardiograms, they would be mistaken for *a*, *c* and *v* waves accompanying each ventricular cycle. The corresponding electrocardiogram is shown in Fig. 17.

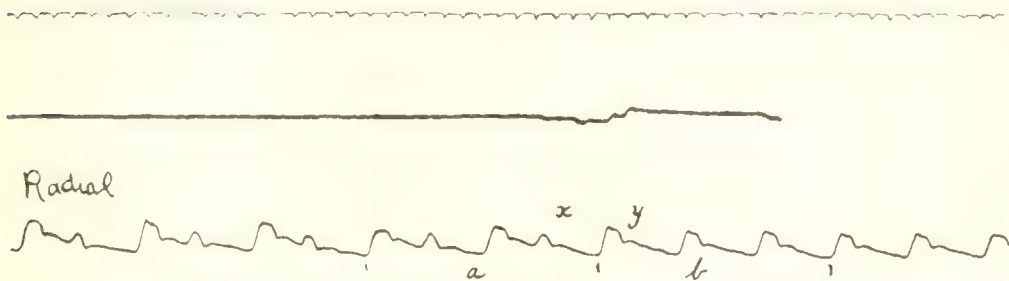


Fig. 7. A radial curve from the same patient, showing the passage from a period of 2:1, 4:1 heart-block into a period of 4:1 heart-block. The interpretation of the curve is known from comparison with such electrocardiograms as that shown in Fig. 16.

The presence of heart-block may be determined from the radial curve itself, by noting the shortness of the pause *x* as compared with the pause *y*, and by noting the equality of the two periods *a* and *b*.

been fully described in the present paper. The radial pulse is beating regularly at 73 per minute, a rate which it maintained for many days. There is little in the venous curve to guide the observer to the true condition of the auricle, which as we know, from the corresponding electrocardiographic curve (Fig. 17), was beating at the time when this curve was taken at the rate

of 292 per minute. Very considerable help may be obtained in the interpretation of such curves from a careful study of arterial tracings. A curve, such as is shown in Fig. 7, does not represent the passage of a period of bigeminy (resulting from premature contractions) into the normal rhythm: if that were so the length of the cycle x would not be conspicuously shorter than the cycle y . Such curves are given by heart-block alone. The clue to the actual mechanism which produced this curve is given by a comparison of the periods a and b . They are exactly equal, yet one contains four cycles while the other contains *three*. Assuming a constant auricular rate throughout, the proportion between the number of responses over the period a and over the period b should be as 4 is to 3. This proportion is only fulfilled by two conditions, (1) the passage of a 1:1, 2:1 ratio into a 2:1 ratio, or by (2) the passage of a 2:1, 4:1 ratio into a 4:1 ratio. One or other of these conditions would, I think, alone account for the curve as it stands. Further than this the analysis could not be taken, upon the evidence of this radial curve alone: but the electrocardiogram taken on the same day, Fig. 16, shows that the second interpretation is the correct one: the mixture of 2:1 and 4:1 periods is clearly demonstrated in this curve.

Thus, the group of cases considered is of importance because, in the absence of electrocardiographic curves, the high frequency of auricular contractions may remain unsuspected. In the case which I have described in detail, the pulse rate was for several days within the normal limits, and usually its rate was 75. Yet the rapid auricular action (280-300) was maintained throughout the whole of this period, and neither the skiagraphic examination of the chest, nor the employment of the polygraph was sufficient to reveal its presence.

Finally, I may again draw attention to the action of the auricle in cases where the rate of its contractions is raised phenomenally. As I have already determined, by an examination of the electrocardiograms of ten patients during the period of tachycardia and by a comparison of these curves with those of normal or quiescent periods the shape of the auricular summits proves that the new rhythm originates, not at the pacemaker, but in some new auricular focus. The same statement applies to instances of tachycardia in which rates of 300 are approached, as shown by the present series. The comparison of the P summits during the period of tachycardia and while the normal mechanism is present is possible in Fig. 17 and 21 and in Fig. 22 and 23. That the site of impulse formation, in the patients from whom Fig. 17 and 23 were obtained, was *ectopic*, is evident from the abnormal shape of the P summits, as compared to the normal, while the tachycardia is present. That it was also ectopic, in the case which is illustrated by Fig. 24, is evident from the outlines of the summits in leads *II* and *III*. In both these leads P is inverted. Similar pictures were obtained from the fourth patient. Electrocardiograms were obtained in Jolly and Ritchie's patient and also in Rihl's: and though a comparison with the curves of the normal mechanism is not possible, where they are concerned, it is probable that in

these instances also, a new site of impulse formation had developed. It consequently seems clear that instances of accelerated auricular action to rates of 250 or 300 are usually, if not always, associated with displacement of the centre of impulse formation. As in patients who exhibit slower paroxysms of tachycardia, the new rhythms are ectopic.

PART II.

ANOMALOUS VENTRICULAR ELECTRIC COMPLEXES OF SUPRAVENTRICULAR ORIGIN: ABERRANT VENTRICULAR CONTRACTIONS.

In previous articles, I have impressed the importance of the principle, that in the interpretation of electrocardiographic tracings, the shape of the curve is controlled by the direction taken by the contraction wave. When an impulse descends to the ventricle along the normal path and enters the musculature of this chamber through the *normal field of reception*, namely, the arborisations of the auriculo-ventricular bundle, the anticipation is that it will give rise to a contraction, which yields a ventricular complex of a definite and recognised form, namely, that which is regarded as physiological. And this anticipation is realised under most circumstances, be they experimental or clinical. But the rule is not without important exceptions. It occasionally happens, as in the case reported at an earlier date,⁷ that impulses which can be shown to be of supraventricular origin give rise to contractions yielding ventricular complexes of anomalous outline.

The case from which the original curves were taken is still under observation and has been repeatedly re-examined. The patient is the subject of paroxysmal tachycardia, and numerous premature contractions of auricular origin interrupt the slow periods. The origin of the premature auricular contractions has remained constant for an observed period of two years. This conclusion is based upon the shape of the electric complex, which represents the prematurely contracting auricle. The usual peak *P*, of the rhythmic beats, is replaced by a small and inverted summit; a summit which has maintained a uniform outline for the period named.*

But while the premature auricular complex has remained uniform, the complex accompanying the succeeding ventricular contraction has been of three distinct forms. For the convenience of description I rename these complexes, types *A*, *B* and *C*. Type *A* is a ventricular complex of normal

* In the original paper, the inverted summit was interpreted to result from an ectopic beat, or one arising at a point lying at a distance from the pacemaker, and this interpretation was based upon experimental observations which have recently been criticised by Rothberger and Winterberg.¹⁴ If various points of the auricular surface are stimulated, the auricular complex is of a different but definite form with each separate stimulation. Rothberger and Winterberg consider that this may be due in some measure to escape of the stimulating current, and state that they have been unable to avoid this escape. Personally I have had no such difficulty since I have used closely approximated electrodes, and may state quite emphatically that such complication of the curves is quite a rare event, but that if it does occur, it is readily recognised, and should not confuse the interpretation of curves.

outline, being of the same shape as the ventricular complex of a rhythmic beat. The ventricular complexes of premature contractions arising in the auricle correspond in most patients to type *A*: an example is shown in Fig. 8 of the present paper. It is to the divergent types that I desire to draw attention at the present time. Types *B* and *C* are shown in Fig. 25. This figure consists of twelve curves, arranged in four vertical columns, each containing the pictures of Einthoven's three leads (marked *I*, *II* and *III* respectively in the figure and arranged in three corresponding horizontal rows). The two central vertical columns (*b* and *c*) of the figure show the curves from the patient already referred to, and the two curves from lead *II* are those originally published. In both curves a couple is shown consisting of a single beat of the normal rhythm and a premature beat. In both instances *T* of the rhythmic beat is notched by the inverted auricular peak (marked *P* below the line), and it is followed by an anomalous ventricular complex. In the particular patient of whom I speak, these anomalous complexes have occurred very frequently, and they have often alternated with each other, from couple to couple.

I have made a large number of observations in the hope of obtaining the corresponding pictures in leads *I* and *III*, but have been only partially successful. There has been no difficulty in obtaining the complete set of six curves; but it has not been easy to identify the curves of leads *I* and *III* with types *B* and *C* as they are seen in lead *II*, for the reason that both types occur in a single patient. When a continuous bigeminy, *including beats of one or other type alone, has been seen*, the lead has been rapidly changed by means of a special key devised for the purpose, and successive strips have been taken of the several leads. In regard to lead *III*, no doubt remains that the beats corresponding to type *B* and *C* of lead *II* are correctly placed in the present figure, but as regards lead *I* this correspondence has not been so conclusively demonstrated, though I believe that here too the arrangement as depicted is the true one. For the time being, we may assume that curves *I*, *II* and *III*, as they are arranged in columns *b* and *c* of Fig. 25, correspond to the complexes *B* and *C* in the respective leads of Einthoven.

I may now describe the curves of columns *a* and *d*. In column *a*, curves from leads *I*, *II* and *III* are shown. They were taken from another case exhibiting paroxysms of tachycardia of auricular origin. In this case, also, anomalous ventricular complexes interrupted the slow periods, and they correspond to the ventricular contractions of beats arising prematurely in the auricle. The premature auricle, in leads *I* and *II*, has much the same form as that of the rhythmic beats; in lead *III* it consists of several small variations. In each lead it is followed by an anomalous ventricular complex, and the shapes of these complexes are very similar to those illustrated by the corresponding leads of column *b*.

Next let us examine column *d*. In this column are three curves from a patient who has been under observation for a year or more. The patient's heart has been irregular as a result of the presence of premature auricular

contractions for the whole of this period. Three leads are shown: each curve consists of two coupled beats, the second of which is premature. The ventricular complexes are anomalous,* though the corresponding contractions are of supraventricular (in this case, auricular) origin. The three pictures of this column (*d*) are very similar to those of column *c*.

Thus three patients have been observed in whom anomalous ventricular complexes have been found to accompany premature auricular contractions: in one (column *a*) the complexes were of type *B*; in another (column *d*) they were of type *C'*; in another (columns *b* and *c*) they were of types *B* and *C*.

Treating the cases singly, the first fact which merits attention is that in all three cases, each repeatedly examined, the type of anomalous complex has been constant.† This constancy of outline from month to month and year to year is especially noteworthy. The mechanism by which such beats are produced is constant, and its constancy suggests its comparative simplicity. The view that the mechanism is a simple one receives additional and strong support when the cases are treated collectively: curves of almost exactly similar type occur in distinct cases.‡

Before proceeding to the statement of a hypothesis by which the occurrence of these anomalous beats may be explained, it may be well to summarize briefly our knowledge of them.

In the present communication it has been stated that (1) they yield uniform electric effects in given patients over long periods, and it has been shown that (2) the same distinctive types are met with in different patients. In a previous communication* I have shown that (3) type *C'* may also occur in experiment and that (4) it is independent of the point of origin of the impulse, providing that the latter arises above the ventricle. (5) The abnormal types are always associated with demonstrable alterations of conduction in the tissues uniting auricle and ventricle. Occasional or continued prolongation of the *P-R* interval has been found in each and all of the patients in whom they have been observed,§ and also in the dog in which they were seen.

The recognition of these conduction changes in the patients considered may necessitate repeated examination. They may not be in evidence at the first or even the second or third examination: but they are eventually found.

A characteristic example of the phenomenon has been recently recorded by my former assistant Dr. Leo Rosenthal.¹³

Surveying these facts, and remembering how the shape of an electric curve is controlled by the direction of the contraction wave, one hypothesis

* The patient presented those anomalous complexes on occasion only. They were usually of type *A* (Fig. 8 & 9 are from the same case).

† Within certain limits to which subsequent reference will be made.

‡ Type *B* has been figured by Kraus and Nicolai.⁶ These authors have attempted to associate it, though upon insufficient grounds, with a beat of atrio-ventricular origin.

§ Five patients altogether. A prolongation of interval is seen in lead *II*, Fig. 25, column *a*, of one of the new cases here described.

alone seems adequate in explanation of them. It is suggested that they may be due to damage affecting *special* branches of the auriculo-ventricular arborisation, and that this damage is such that a block is present: so that, at one time, the impulse is transmitted through the whole arborisation, while at other times, it passes into the arborisation, but fails to course along certain given channels.

But before this hypothesis can be accepted, an observation remains, with which it must be reconciled. A series of curves was published from the original case, in a previous article to this journal,⁸ which showed a complete transition from the normal type (type *A*) to type *C*. I am now able to publish a second though less perfect series. Two curves are shown in Fig. 26. They are from the same case as those of column *d* of the last figure. Both are from lead *II*. The second and premature beat of the top curve in Fig. 26 has a ventricular complex of type *A*. The premature beat of the bottom curve (Fig. 26) is transitional between type *A* and type *C* (Fig. 25, column *d*, lead *II*). Special attention is drawn to the intervals in these three curves. *Proceeding from type A to type C, the prematurity of the second beat of the couple increases; the shorter the interval intervening between normal and anomalous beats, the greater is the divergence of type.* A precisely similar observation was made in the instance formerly published;⁸ and the anomalous beats were seen in experiment, only when this interval was short. We may continue the previous summary by stating that (6) the anomalous beats show transitions and that (7) they are most in evidence when the ventricular contractions to which they belong follow the preceding contractions at short intervals.*

The prematurity of the contraction influences the type of complex because the recovery of conduction is dependent upon the interval of rest which precedes the contraction with which it is associated.

How may the transition types be explained? I assume that a given anomalous complex, in its fully developed form, results from a complete obstruction to the passage of the impulse along certain definite branches of the arborisation. The transition forms are explained if it is assumed that during the progress of certain beats, there is delay in the passage of the impulse along the same branches of the arborisation; and according as the delay is small or great, so the complex will approach more closely to type *A* or type *C*.

I may illustrate and support this conception by describing the accompanying figure, an experimental curve. Fig. 27 shows myocardiograms (*A* and *V*) from auricle and ventricle respectively, an electrocardiogram, a time-marker and signal of stimulation. The stimulation was repeated at rhythmic intervals, the rate of stimulation being slightly in excess of the heart rate, and the point of application being the left margin of the ventricle

* Similar changes accompany increase of heart rate, notably in paroxysms of tachycardia: a fact which has been discussed in my book "The Mechanism of the Heart Beat," London, 1911, page 180.

near its apex. The first two stimuli fall, as shown by the vertical lines drawn from the signal, in the refractory period of the ventricle. The third falls just before the commencement of the refractory state; the fourth a little earlier and so on. Each falls *subsequent to the commencement of an auricular contraction*. Thus in each cycle two contractions waves are started, one naturally and from the auricle, the other artificially and from the apex of the ventricle. According as one or other is precedent so it governs the ultimate type of the ventricular contraction. In the fourth cycle of the figure, the ventricular contraction is almost a pure response to the supraventricular impulse. In the last cycle of the figure, the ventricular contraction is a pure response to apical stimulation. Between them lies a perfect transition series, and this transition series is the result of a gradual alteration of the times at which the impulses reach the several portions of the ventricular muscle mass. A gradually increasing delay in the conduction of purely supraventricular impulses, through a limited division of the arborisation, will produce a comparable series of transition curves: and such is the explanation offered of the clinical electrocardiograms which have been discussed.

As final illustrations of the phenomenon for which I propose the term "aberration of the supraventricular impulse" or "aberration" I may cite certain experiments upon asphyxial heart-block.

In conjunction with Mathison⁹ I have shown that all the known stages of auriculo-ventricular heart-block may be produced in cats by a simple process of asphyxiation, but we were unable to demonstrate that the block is produced as a result of poisoning of the special junctional tissues. Evidence for this is now forthcoming, thanks to the observations of Eppinger and Rothberger.² These workers have demonstrated that separate section of the left and right main branches of the auriculo-ventricular bundle is followed by beats of the ventricle which start in right or left ventricle, respectively. Such beats, which are unquestionably aberrant, in the sense in which I use the term, give rise to electric curves, which correspond to the recognised complexes of premature ventricular beats, started in the right and basal portion of the heart or left and apical portion of the heart respectively.

It not infrequently happens that similar pictures are obtained from the asphyxiated cat. Perhaps, as in Fig. 28, 2:1 heart-block is present, when suddenly the normal ventricular complex gives place to one which is recognised as corresponding to a contraction started in one or other side of the heart (in the instance figured it is from the right and basal portion of the ventricle).^{*} Very many interesting curves are produced in this manner and they suggest that the products of asphyxia act, not only on the junctional tissues as a whole, but also to a varying extent on the several portions of this system. Transitional curves between the normal and a fully aberrant type

^{*} Very similar curves have been recently published by Einthoven, who produced them experimentally by stimulating the vagus.

are surely to be anticipated under these circumstances, and I publish the last figure as a probable example of the phenomenon. The curve shows the passage of a period in which there is prolongation of the *P-R* interval to what is apparently complete dissociation. The type of ventricular complex suddenly changes from the normal (*R, T*) to that of a beat starting in the left or apical portions of the ventricle. From this point onwards there is a complete transition from the large diphasic complex to the normal complex, which is seen at the end of the curve. In explanation of this curve I suggest first that at the point of the primary change, complete dissociation supervened as a result of poisoning of the main bundle; and that the bundle directly below the seat of functional damage became at that moment pacemaker to the ventricle. So far the explanation is in accord with all previous observation. I suggest further that the mechanism was complicated by the simultaneous onset of functional damage to the right branch of the bundle. The first impulse discharged from the ventricular pacemaker consequently travelled along the *left* branch alone. At the second discharge, the impulse travelled along the left branch, and after considerable delay, also along the right branch. At the third discharge the delay in the right branch was less, at the fourth less still, until at the discharge which created the last beat represented in the curve, conduction was again equal on the two sides.

SUMMARY OF PART I.

1. The auricular contraction which follows a premature auricular contraction, may arise from the same focus as the premature beat. The phenomenon is considered to be the result of slight quickening of physiological impulse formation in the area in which the premature beat arises. (Section 1.)

2. A clinical instance of premature auricular contractions, followed by pauses, which are considerably shorter than the interval between rhythmic beats, is described. It is probable that the premature beats originated in, or near, the pacemaker; the shortening is referred to acceleration of impulse formation in the pacemaker, as a result of the origin of premature beats in it, or in its neighbourhood. (Section 2.)

3. The direct and repeated change of regular and accelerated auricular action to auricular fibrillation and back again is recorded (Section 3). Another case, in which an ectopic auricular rhythm was converted into fibrillation by the action of digitalis, receives detailed description (Section 4). Several additional cases of a similar nature are described (Section 4). The observations show the close inter-relation of paroxysms of regular tachycardia, arising in the auricle, and auricular fibrillation.

4. An instance of auricular fibrillation, in which the ventricle beat at 90 per minute, and in which its action was perfectly regular, is placed on record. The regularity of the ventricular action is ascribed to the presence of complete heart-block, brought about by digitalis administration. Another, and somewhat similar case, is referred to (Section 3).

5. An instance of unexpected death in a patient, whose curves had shown auricular fibrillation and premature ventricular contractions a few hours previously, is recorded. Death is attributed to ventricular fibrillation. (Section 3.)

6. A patient who came under observation with a ventricular rate of 150, and an auricular rate of 300, is recorded; electrocardiograms from two similar cases, in both of which 2:1 heart-block was present, and in which the rate of auricular contractions reached 320 and 315 per minute, are also described. Extreme acceleration of the auricle, to 300 per minute, does not seem to be an uncommon condition; several other instances are spoken of. Heart-block usually accompanies the condition, so that the acceleration in the ventricle is not of like degree. (Section 4.)

7. The exact doubling of rate in paroxysmal tachycardia, described by Hoffmann, is probably referable to the relief of heart-block of 2:1 grade. (Section 4.)

8. Extreme acceleration of the auricular rate usually gives place, sooner or later, and especially as a reaction to digitalis, to fibrillation. The normal rhythm is often restored subsequently. Digitalis medication is of considerable value in such cases, either by reducing the ventricular rate, or by ultimately aiding the restoration of the normal rhythm. (Section 4.)

9. When auricular acceleration is accompanied by heart-block, and fibrillation sets in, at the onset of the latter the ventricular rate is lowered. (Section 4.)

10. Extreme acceleration of the auricular contraction rate is the result of new and ectopic impulse formation in that chamber. Four new examples are cited as evidence of this statement. (Section 4.)

11. The polygraphic curves obtained from patients, in whom the auricular contraction rate shows extreme acceleration, are often deceptive. They may easily be mistaken for curves given by a normally beating heart; the electrocardiographic examination may be the sole means of detecting the true nature of the heart's mechanism. (Section 4.)

12. An instance of pressure upon the right vagus nerve is described, in which heart-block was the sole result. The auricles continued to beat at the original rate, which was an extremely accelerated one.

SUMMARY OF PART II.

1. Several examples of anomalous electric complexes, accompanying the ventricular contractions of premature beats arising in the auricle, are described. It is shown that the anomalous complexes may be classed as distinct types, for the same types are encountered in separate individuals. This fact and the uniformity of their appearance in electric curves taken from isolated cases, from month to month and year to year, suggests that the mechanism of production is a comparatively simple one. In view of their constant association with demonstrable conduction changes in the

auriculo-ventricular junctional system as a whole, the hypothesis is put forward that they are due to disturbances of conduction in the smaller branches of this system; and it is held that definite branches are affected in this manner, though these branches cannot be identified at the present time.

It is proposed that the phenomena discussed should be termed "aberration of the supraventricular impulses" or more simply "aberration"; the anomalous beats may be conveniently spoken of as "aberrant beats" or "aberrant ventricular contractions."

2. There seems every prospect that, if this hypothesis be correct, it will be possible ultimately to identify lesions which affect not only the main divisions, but the smaller branches of the auriculo-ventricular bundle.

3. The products of asphyxia probably act in a selective manner upon the special tissues which serve the function of conducting impulses from auricle to ventricle.

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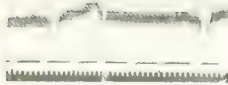


Fig. 8
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Fig. 9
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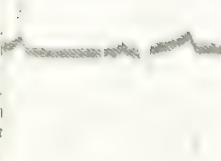


Fig. 10
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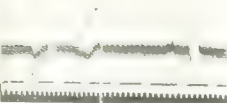


Fig. 11
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Fig. 12
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Fig. 13
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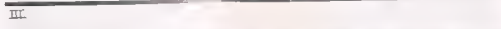
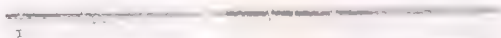
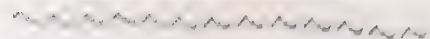
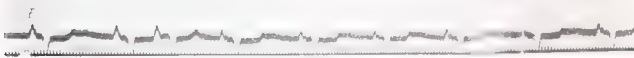
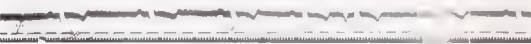
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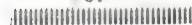
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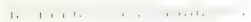
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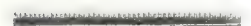
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1



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Fig. 10. The first group of the test with the sinus node. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve.

Fig. 11. The second group of the test with the sinus node. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve.

Fig. 12. The third group of the test with the sinus node. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve.

Fig. 13. The fourth group of the test with the sinus node. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve. The sinus node is the first to be affected by the vagus nerve.

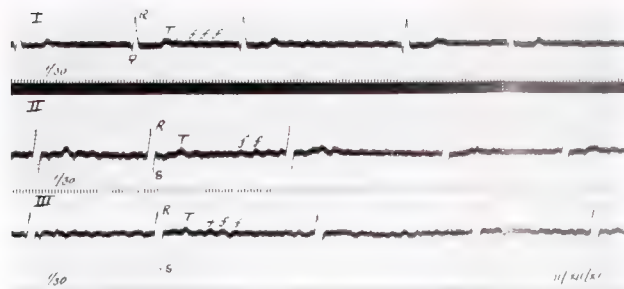


Fig. 10

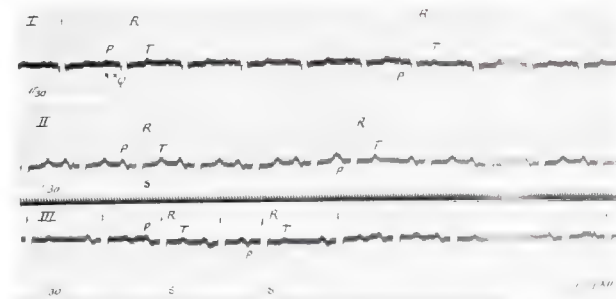


Fig. 11



Fig. 12

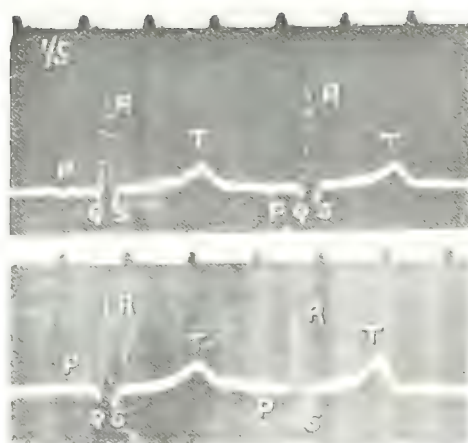
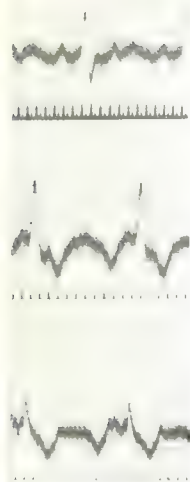


Fig. 26

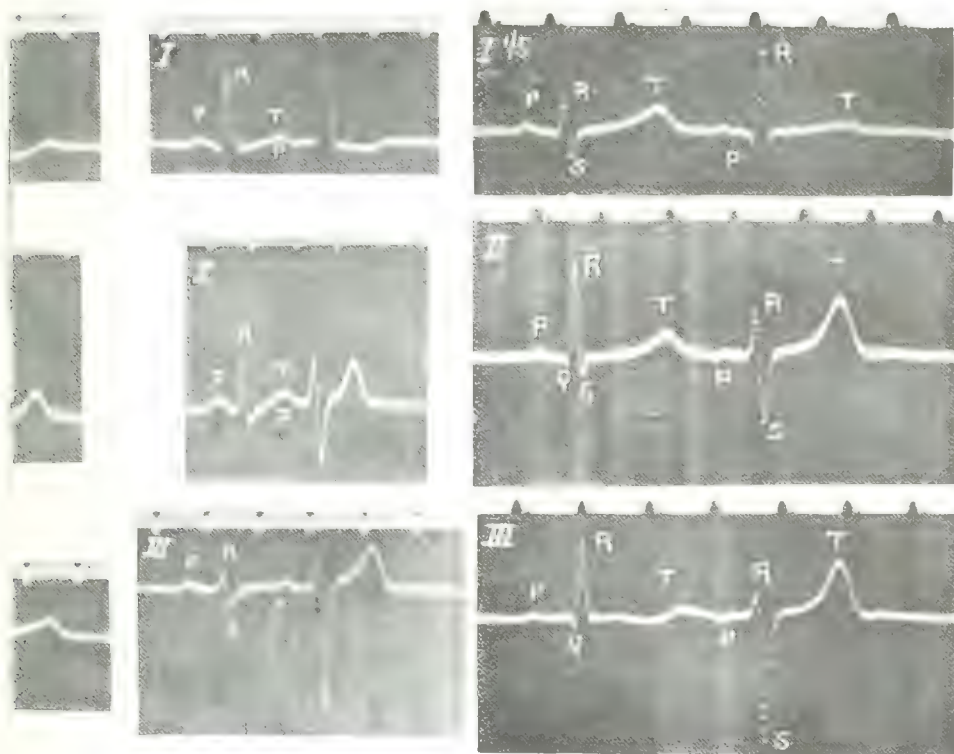
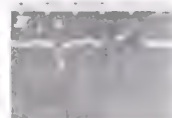
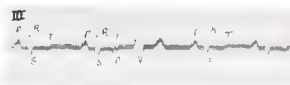
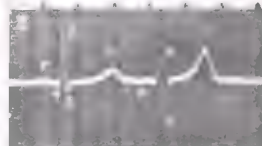
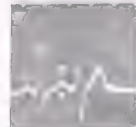
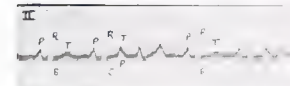
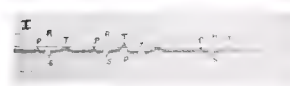
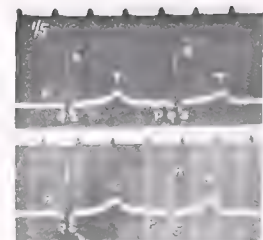
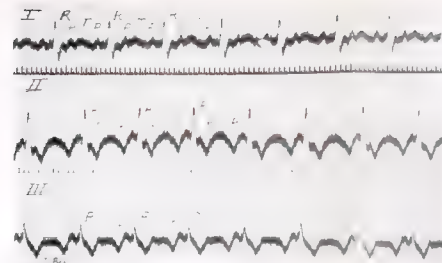


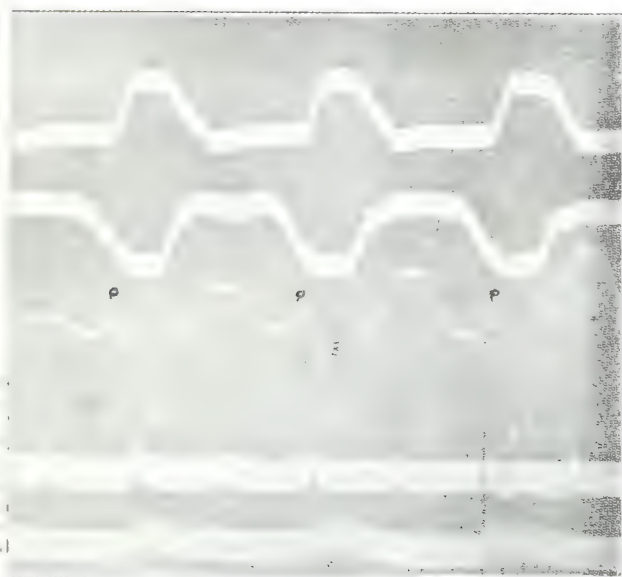
Fig. 25

the heart, and the heart is not able to pump out the blood as fast as it is coming in. The blood then backs up in the veins, and the heart is unable to pump it out. This is called congestive heart failure.

The heart is a muscle, and like all muscles, it can become weak. When the heart is weak, it cannot pump out the blood as fast as it is coming in. The blood then backs up in the veins, and the heart is unable to pump it out. This is called congestive heart failure. The heart is a muscle, and like all muscles, it can become weak. When the heart is weak, it cannot pump out the blood as fast as it is coming in. The blood then backs up in the veins, and the heart is unable to pump it out. This is called congestive heart failure.

A heart that is weak is called a weak heart. A weak heart is not able to pump out the blood as fast as it is coming in. The blood then backs up in the veins, and the heart is unable to pump it out. This is called congestive heart failure.





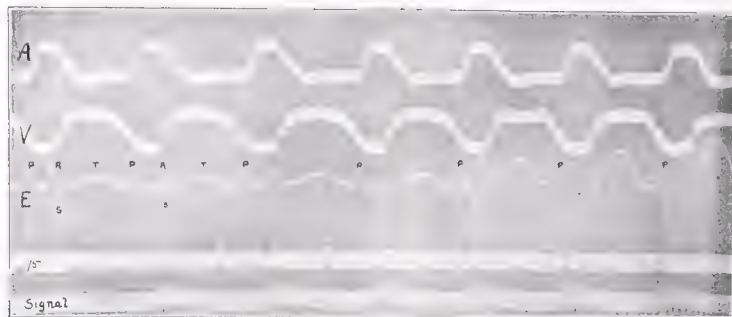
27. Record of
lead II, III, and
aVF. The P waves
are slightly
abnormal in shape.
The rhythm is
normal.

28. An ECG
tracing. The
rhythm is normal.
The P waves are
normal.



29. An ECG
tracing. The
P waves are
normal. The
rhythm is normal.
The P waves are
normal.





OBSERVATIONS ON THE FUNCTIONS OF THE SINO-AURICULAR NODE IN THE DOG.

BY ALFRED E. COHN, LEO KESSEL AND HOWARD H. MASON.

*(From the Department of Pathology, College of Physicians and Surgeons,
Columbia University, New York.)*

1. *Introduction.*

A preliminary notice of the experiments to be detailed here appeared in February, 1911.² To the fourteen experiments then briefly reported, sixteen have now been added. The latter have substantiated the results of the earlier ones and have added new facts. At that time earlier and similar experiments were reviewed. Additions have since been made to this subject of which we shall make brief mention here.

The sino-auricular node, described by Keith and Flack¹¹ in April 1907 and substantiated by Koch¹³ in 1909 is now well known. Before the publication of these communications, experiments had been conducted with the view of studying the location of stimulus production by Adam in 1906,¹ Langendorff and Lehmann in 1906,¹⁵ Erlanger and Blackman in 1907,⁴ and Hering in 1907-1909.^{7, 8} When the first experiments of the present series were completed in August 1910 it seemed desirable to report them, because none had been published in which the newly discovered anatomical facts had been considered.

Adam had found that he was able to obtain prompt changes in the rate of the heart by quickly changing the temperature of that area of the heart which lies between the entrances to the auricle of the venæ cavæ, more especially that near the inferior vena cava. Langendorff and Lehmann continued these observations by experiments on the excised hearts of rabbits perfused with Locke's solution. It was their intention to excise the stimulus producing area in the right auricle and although areas including the superior vena cava, inferior vena cava and tænia terminalis were excised, we are not able to conclude whether the areas excised included the area now known to contain the node. They found that after the areas mentioned had been removed, the auricles ceased to contract, while the ventricles after a temporary cessation, began to contract again, but at a much slower rate. If their perfusion fluid contained defibrinated blood, the hearts did not stop.

Erlanger and Blackman also worked with the hearts of perfused rabbits. They state (p. 133) that the amount of tissue excised varied in different experiments, as did also the location from which the pieces were removed.

In their experiments, the auricles unlike those in the experiments of Langendorff and Lehmann, but like those in the present series, continued to contract after operation. This difference may be due to the fact that either the correct portion or the correct amount had not been removed. Experiments to illustrate these points are detailed later in this communication. They found also that the dominance of the auricles or ventricles varied after the operative manipulation, and similar results will be found in these experiments.

Finally Hering, on the evidence gained from inspecting the dying heart, thought that the last portion to cease contracting was that at the entrance of the superior vena cava, sometimes the portion about the inferior vena cava, and that in any case the right auricular appendix judged by this criterion was never involved in stimulus production. He was able to cut away the region of the right auricle at the entrances of the venæ cavæ, making a wide incision, and found that the right auricle still continued to beat with regularity. He does not mention at what rate the heart beat after operation (p. 145). He was of the opinion that not all supraventricular portions were capable of automatism and certainly not the left auricle, but he did not give an exact site for this activity. He mentioned the fact that an incision 1 cm. long, along the *sulcus terminalis*, sufficed in many cases to terminate the contractions of supraventricular portions of the heart. We will discuss this point later.

Additional papers on the subject have appeared by Jaeger,¹⁰ Magnus-Alsleben,¹⁵ Wybauw,²¹ Lewis,¹⁶ Lewis and Oppenheimer,¹⁷ Hering and Koch,⁹ and Flack.^{5, 6}

Jaeger employed the method of scorching the area supposed to be the site of the node. He observed the effect obtained experimentally and then examined the scorched area in serial sections. He found that the structure of the node was disturbed, but that the damage which had been done to it, did not result in any disturbance of the rhythm. He showed a curve to illustrate this statement. He stated that in cats and dogs the node is useless as a pacemaker, and concluded that other experiments were necessary to discover the significance of this structure. He published a photograph showing an area of destruction of the superficies of the heart which seemed to have involved the sinus bearing area. He has reproduced one curve but no histological sections.

Less significance must be attached to these experiments of Jaeger's in view of those done by Lewis, and Lewis and Oppenheimer, which were exceedingly careful both in technic and in presentation, and which arrived at a different conclusion. Lewis was able to show by means of induction shocks applied to various regions of the auricular wall, that only those which stimulated the area bearing the sinus node elicited electrical complexes comparable to those observed as the result of normal stimulus production. The stimulation of other areas caused contractions, the electrical complexes of which were quite abnormal. Later in his experiments with Oppenheimer he discovered that the only area in which primary electrical negativity was found

was that area afterwards proved on the examination of serial sections to contain the sino-auricular node. For the details of these well planned experiments, the reader is referred to the original paper.

The experiments of Wybauw²¹ were carried out at about the same time as Lewis's. They are published in less detail but are valuable because of the corroboration they lend to those of Lewis. He employed methods similar to Lewis's and arrived at similar conclusions.

Flack performed a series of experiments at Berne, and obtained results similar to those of Adam. He went further and demonstrated that it was through the sino-auricular node that the nerves to the heart, both vagi and accelerators, exercised their functions. In some experiments he applied muscarine and atropine to it, he froze it with ethyl chloride, and in others he clamped it. Then he stimulated the two vagi and sometimes the two accelerators and found that they had lost the effect they had formerly exercised. The results obtained were not quite uniform, but the experiments are suggestive. More experiments might profitably be performed on his plan.

Later still he performed additional experiments in Fredericq's laboratory where he found that he was unable to stop the hearts of rabbits and dogs by clamping the sino-auricular node and was able to slow the auricular rate only slightly. He has called attention to the difference between his results and those published by us.² It must be remembered that his experiments were carried out on hearts beating *in situ*, with normal nutrition. The difference in method may be responsible for the different results obtained in the two sets of experiments. Later experiments have convinced us that this is so. But much information about the function of the node has been obtained in a number of ways, and we believe that the method of perfusion which we have employed adds some evidence in favour of the pacemaking function of the node.

Another method of studying the same subject is that of Hering.⁹ After scorching the area of the sino-auricular node and after cutting both vagi, he estimated the *As-Vs* interval. His purpose was to observe whether a heterotopic site of stimulus production arose, resulting in a shortened *As-Vs* interval. He succeeded in producing this shortening and in this his experiment succeeded. But whether scorching the sinus area influenced the rate of the heart cannot be determined because the rate of the heart before this procedure is not mentioned. Koch examined serial sections made from these hearts. He reports (p. 482) that the pericardium was damaged but that little injury had been done to the muscle.

Magnus-Alsleben¹⁸ performed his experiments on the node in the hearts of rabbits perfused with Ringer's solution two parts, and ox blood one part. He registered only the right ventricle. No histological reports are published so that it is difficult to state exactly what he excised, the more so because in Experiment 1 he says that bits of the auricles ("*Fetzen der Ohren*") were left behind and in Experiment 2, the superior vena cava. He denies

that the sino-auricular node is a pacemaker. He concludes that the sinus area and another one in the wall of the right auricle set a somewhat faster pace. If these areas are removed, a temporary disturbance takes place. He maintains that all parts of the auricles have the same grade of stimulus production, although at the lower levels the rate is somewhat slower.

His results are quite opposed to those to be found stated in the present communication. He used rabbits except in one experiment where he used a dog; in this experiment he got slowing of the ventricular rate. Unfortunately only two pairs of curves are shown in which both auricles and ventricles are registered and few details of the experiment are mentioned. Further on in our communication it will be seen how important the histological controls are, and Magnus-Alsleben has left us entirely without them.

II. *Methods of experimentation.*

In these experiments dogs were used. On account of the nature of the perfusion apparatus, only dogs of small or medium size could be employed. They were completely anesthetized with ether and were then bled. In eighteen experiments (557 to 565, 567, and 569 to 578), the chest was opened, the heart was excised and tied to and suspended from the cannula of the perfusion apparatus. This portion of the apparatus was surrounded by an inverted bell-jar. A hook fastened in the left auricle was connected by a thread which passed through an opening in the side of the bell-jar to the membrane of a receiving tambour. A similar hook was inserted into the right ventricle near the apex, a thread from which directed downward through an opening in the bottom of the inverted bell-jar passed over a small wheel and proceeded at right angles to the membrane of a second receiving tambour. In twelve other experiments (579 to 590), the dogs were bled, the chest was opened, the heart was left *in situ* and the cannula of the perfusion apparatus was passed into the ascending aorta. A ligature was tied round the arch of the aorta below the point at which the vessels to the fore legs and neck are given off; sometimes the latter were secured by special ligatures. The inferior vena cava was incised in the abdomen. The pericardium was laid open and sewn back to the cut edges of the ribs. Hooks were inserted in the right auricle and right ventricle, which were fastened by strings to two receiving tambours, each held by a stand in a position suitable to the free play of the strings. In each of the arrangements described, the receiving tambours communicated by means of air transmission to two writing tambours, the tambour recording auricular contraction being placed in each instance above that writing ventricular contraction. The writing tambours were supplied with pens, which wrote with ink on white paper. This made it possible to take continuous records of any length, the inscriptions continuing in most of the experiments during all the experimental manipulations.

The hearts in all these experiments were perfused with Locke's solution, at a temperature of 29 to 33 degrees, the temperature varying within these limits from one experiment to another. The pressure employed was usually 40 mm. Hg.. Pressure and temperature were ascertained at a point just before the insertion of the cannula into the aorta by means of two side arms, one of which contained a thermometer which lay in the perfusion stream while the other communicated by means of pressure tubing with a mercury manometer. Pressure could be varied by changing the level of the eight litre reservoir. No experiment was undertaken unless the heart was beating regularly and, with the exceptions noted later, co-ordinately.

An effort was made to excise the sino-auricular node with the slightest possible loss of auricular tissue. In most instances this was accomplished. Occasionally, however, on account of the variation in the anatomy of the node, both as to size and site, more tissue was excised than was necessary. With the exception of five experiments (557, 558, 559, 560, 571), the node was excised in two stages, as follows (see Fig. 1). Incision 1 was



FIG. 1. In this and the succeeding figures, S.V.C. is the superior vena cava; I.V.C. is the inferior vena cava; R.A.A. is the right auricular appendix. The order of the cuts made in the excision of the node is indicated by the numbers, 1, 2, 3 and 4.

made at the point of junction of the superior vena cava with the upper border of the right auricular appendix, across the upper end of the sulcus (tænia) terminalis. This was followed by incisions 2 and 3, lying respectively to the right and to the left of the sulcus and parallel with it. After these three incisions had been made, curves were taken. In addition curves were sometimes taken between incisions 1 and 2, and 2 and 3. A final incision 4, joining the lower extremities of incisions 2 and 3, effected the excision of the node. While the incisions usually corresponded to this type, there were seven experiments (564, 569, 570, 580, 581, 583 and 585) in which it was necessary to remove additional pieces: one (579), in which the incisions were made in the opposite direction (4, 2, 3, 1); and two (584 and 586) in which a further operation consisted in the extension of one incision to the A-V groove.

The pieces excised were put aside in a dish of Locke's solution, during the period of the experiment, and were afterwards sewn on to cards to preserve

their shape; the edges were designated superior, inferior, &c., to facilitate their subsequent identification. It was found that directly after removal, this node bearing area contracted to half its original size. The pieces so obtained, together with the hearts themselves were fixed in formol-Mueller (1-9) solution, washed and preserved in 70 per cent. alcohol. The method of imbedding, cutting and staining, is described in a previous communication³ (p. 245). In each case all the sections, cut in series at ten micra, were preserved and mounted. Calculations of the length of the node were made by computing the number of sections.

The *position* usually assigned to the node, at the junction of the superior vena cava and the upper border of the right auricular appendix, was found to be very serviceable. It must be noted though, that sometimes it begins higher, and at others lower, along the sulcus terminalis. Occasionally (as in 564, 584), it lies in part in the wall of the superior vena cava, so that incisions planned in the ordinary fashion fail to include the node. At other times it lies unusually far to the right, near the attachment of the pericardium (see Fig. 5). It is due to variations such as these, that the outcome of excision experiments cannot always be accurately predicted. Since the whole heart, as well as the sinus bearing area, was invariably preserved, it was possible in many cases, where the node was not found, either in whole or in part, in the portions excised at operation, to cut additional pieces from the hearts in series, so as to estimate how much nodal tissue had been left behind, and in what situation. This cutting of portions left behind served to clarify the results of many experiments which would otherwise have remained obscure. It must be noted that on account of unequal retraction of the layers of the walls of the heart and the superior vena cava, exact identification of the contiguity of the cut edges was very difficult and sometimes impossible. But although the fitting of the cut edges to each other may have been desirable, enough could be learned to provide satisfactory explanations of the experiments. For the histological details reference should be made to the protocols.

It will be clear from the foregoing account that in this series and in spite of care, the node was, in many instances, not excised in its entirety, either in the first or in subsequent attempts. These failures are interesting as controls to the cases where the node was completely removed, and for the many valuable side lights which they throw upon the other experiments.

The largest node in this series measured only 8 mm. (8,000 micra) in length, while the greater number were but 4 or 5 mm. (4,000 to 5,000 micra). Koch¹³ and Lewis and Oppenheimer¹⁷ in reporting upon the *size* of nodes examined by them, found them to be from 10 to 20 mm. in length, but in these the hearts were fixed with the node bearing area *in situ*, and while shrinkage of some degree must have taken place, the amount could not have been so great as in the small pieces preserved from the hearts in these experiments. The difference in method accounts no doubt for the smaller measurements of the nodes in this series. A computation of the square

area of the node at any given level is omitted, for obviously such measurements would not give useful data for comparison under these circumstances.

The nodes in the sections from the pieces excised were easily identified. The *structure* corresponded closely to the published descriptions. While the general characteristics of nodal tissue are easily recognisable, the variations from type are of interest. The site of the node in a dog's heart varies; it is always found in fairly close relation to the tænia terminalis, and is sometimes included within it, but more often it is found directly to the right of this structure or some little distance from it. The mass of tissue of which the node is composed varies considerably at the point of its greatest diameter; sometimes its bulk is relatively large, while at others it is attenuated. It usually lies under the pericardium and is separated from the endocardium by a considerable layer of auricular muscle. Not infrequently, however, it occupies the entire space between endocardium and pericardium. Although the node is usually found under the pericardium above, at its lower levels it lies somewhere between endo- and pericardium, lost in auricular muscle but never directly under the pericardium. Lewis and Oppenheimer¹⁷ describe the node as being club-shaped. It seems, however, to taper at the ends, more especially at the lower end, so that it appears like an irregular inverted cone, with a long tapering apex. Another criterion for identification has been the presence of an artery first insisted on by Koch.¹³ In the nodes examined, a large vessel was usually present; occasionally it is represented by several smaller ones, and rarely it is absent. Occasionally, also, the larger vessel lies in relation to the node in its lower levels alone. The thickness of the overlying pericardium and the amount of connective tissue found within the body of the node is variable. The pericardium at this point is usually, but not always, thicker over the node than elsewhere. Nerve fibres and ganglia are constantly found in the node, although the number of fibres and ganglion cells varies considerably.

III. *General summary of results.*

In all, thirty experiments were performed in which the sinus bearing area was excised. Of these, seven experiments (577, 578, 579, 587, 588, 589 and 590) were undertaken after other manipulations had been carried out. These constitute the experiments in groups *B* and *C* in the table on page 342. In these seven experiments, the auricles alone were contracting, for fibrillation of the ventricles had occurred spontaneously or had been induced by faradization. The fact that the ventricles were fibrillating in these cases does not detract from the value of the demonstration of the control of the rhythm and rate of the auricles by the sino-auricular node. In fact an interesting side light is thrown upon the subject of such control, notably in Experiment 588.

The plan for excising the sinus bearing area (*i.e.*, by means of four incisions, with an interval between the third and fourth incisions), will be

remembered. The effect usually noted after the excision of the node was *stoppage* of the whole heart. In the thirty experiments stoppage after the fourth incision occurred in twenty-four. In the remaining six, stoppage was not determined. In two (557 and 558) there is no note referring to it in the protocols, but there was a reduction in rate from 114 to 81.9 or 31.1 beats per minute and from 121.5 to 63 or 58.5 beats per minute respectively. In a third experiment (577) although there was no stoppage, the occurrences during the experiment indicate that the node had been excised. In the twenty-four experiments, and also in the three additional ones (557, 558, 577), the sino-auricular node had been completely, or almost completely, excised. That is to say in 90 per cent. of the cases stoppage, or its equivalent, occurred after the node had been removed either entirely or in greater part.

Of the remaining three experiments (562, 563 and 570) in which no stoppage is recorded, the auricular rate increased 30.6 in one and fell 3.6 and 43.5 per minute respectively, in the others. In No. 562, there was no stoppage, although the node was probably excised in greater part (6,040 micra): the same is to be noted of No. 570, where, after the excision of 8,760 micra, it seems unlikely that much of the node could have been left behind. In No. 563, however, only 2,990 micra were excised, enough of the node remaining to explain why stoppage did not occur. It will be seen in examining Table 1 that although in other experiments (576, 579, 582 and 590) stoppage occurred when amounts of nodal tissue as small as that in No. 563 (2,990 micra) were taken out, the excision of amounts as large as those removed in No. 562 and 570 (6,040 and 8,760 micra) invariably produced a stoppage.

Thus there are discrepancies between the amount of nodal tissue removed and the results of such removals. But, on the whole, it may be said, in spite of the three exceptions, that when the greater part of the node is removed, a stoppage of the heart takes place and, as will be pointed out later, a reduction in rate ensues. There were actually ten experiments (Table 1, *Ic*) in which small amounts of node were left behind, without altering the result, namely the occurrence of stoppage or its equivalent. But sometimes when similar small amounts were left behind stoppage did not occur. Inconsistent results of a like nature have been observed in dividing the *A-V* bundle, and they, too, remain unexplained. The method employed, the perfusion, the trauma, the disturbance of the circulation with consequent oedema or anaemia of the tissues, may serve as partial explanations. It is probable that, under varying conditions, at one time a small part of nodal tissue with a good nutrient supply may be functionally sufficient, while at another time a large amount in the absence of such supply may be insufficient. But it must be urged, that, despite the untoward conditions (it is hoped at a later day to report similar experiments with a normal circulation), the uniformity in 80 to 90 per cent. of the experiments is remarkable.

The *stoppage time* varied within wide limits. The shortest time noted was 4 seconds; the longest, 3 minutes. Stoppage of less than 10 seconds

occurred in six experiments: between 10 and 20 seconds in four: between 20 and 30 seconds in seven: between 30 and 40 seconds in two: between 40 and 50 seconds in one: while in the four others, stoppage lasted 65 seconds in No. 585; 92 seconds in No. 572; 117.5 seconds in No. 576; and 180 seconds in No. 589. It will be seen that the heart usually ceased to beat for 30 seconds or less (17 experiments). Occasionally, the interval between the first and second contractions, after the excision of the node, was greater than the stoppage itself. There can be little doubt that the stoppage occurs because a certain amount of time is required before the auricle or some other structure takes up the pacemaking function.

Simple incisions in the neighbourhood of the sinus-node usually *increase* the rate. It will be remembered that curves were obtained after the third incision. In the first four experiments (557, 558, 559, 560) and in two later ones (571 and 579) the experiments were so performed that accelerations after these incisions could not be estimated. In the remaining twenty-four experiments in which an estimation of the rate after the first three incisions could be made, an acceleration was noted in twenty-two. The exceptional cases (570 and 586) in which there was no increase, but a decrease in rate, will be considered later. The lowest rate of acceleration was 0.33 per minute in No. 590, while the highest rate was 50.4 in No. 565. The acceleration was below ten beats per minute in sixteen experiments (562, 563, 564, 575, 576, 577, 580, 581, 582, 583, 584, 585, 587, 588, 589 and 590); it was between 10 and 20 beats in No. 578, between 20 and 30 beats in Nos. 567 and 572, between 30 and 40 beats in Nos. 561 and 569 and between 50 and 60 beats in No. 565. In view of the acceleration which took place in by far the greater number of the available experiments, it seems extremely unlikely that a simple incision, or even multiple incisions in the region of the sino-auricular node, no matter how placed, can be held responsible for the stoppage phenomenon. To bring about this result, total or partial excision is necessary. It may be that the proper incision has not been made to effect the result claimed by Hering,⁷ that an incision alone in this area causes stoppage, and it may be urged, that there are three experiments (564, 584, 586) even in this series where such a result has been obtained. But it is certain that the conditions in these three cases are special ones. If the result in them was due to the incision practised, then it is curious that the same result should not have occurred in more of the remaining experiments. This consideration emphasises the fact that an incision in itself cannot be held accountable for the stoppage phenomenon, providing that it lies outside the node.

But there are a number of experiments in which incisions traverse the body of the node itself. Eleven experiments (563, 569, 570, 576, 577, 582, 583, 584, 585, 588 and 589) present these conditions. Stoppage did not take place, while in ten cases acceleration in auricular rate occurred. Incisions may be made, therefore, both in the neighbourhood of the node, and through the body of the node itself, without causing stoppage. In view of these results Hering's are difficult to understand.

Excision of the node effects not only a stoppage, but a *decrease in the rate* takes place after the primary effects of the excision have passed away. It has been said that there were twenty-four experiments in which the heart stopped after the node had been excised, and to these three others (557, 558 and 577) were added, for reasons already mentioned, making twenty-seven in all. In all but one of these (588), that is to say in twenty-six, the rate fell. It fell less than ten beats per minute in three experiments; between 10 and 20 beats in three; between 30 and 40 beats in seven; between 40 and 50 in seven; between 50 and 60 beats in three; between 60 and 70 beats in four. In twenty-one experiments, therefore, the rate fell more than 30 beats.

From the point of view of reduced rate, three experiments must still be considered. They differ from the preceding twenty-seven because there was no stoppage. In No. 562, the rate *rose* 30.6 beats (57.9 to 88.5); though a piece of tissue bearing 6,040 micra of node was removed, the node had not been entirely excised. In No. 563, the rate fell only 3.6 beats (88.5 to 84.9); that is to say, there was no conspicuous change as a result of the excision; a considerable portion of the node was subsequently found to have been left behind. In No. 570, the rate fell 43.5 beats (118.5 to 75); it fell to a rate which is higher than that usually obtaining after excision of the node. Although 8,760 micra of node were excised, it is possible that nodal tissue in sufficient quantity to prevent stoppage and to maintain the rate at 75 had been left behind. No. 588 is added at this point, although there was stoppage, for the rate *rose* 3.15 beats (50.1 to 53.25). This rise cannot be considered significant, for the ventricles were in fibrillation and the auricles beat irregularly in response to the fibrillating ventricles.* It may be said, therefore, that an excision of the node causes a decrease in the rate of the heart, except in cases where good reason for a contrary result can be found.

There were seven experiments (564, 569, 570, 580, 581, 583 and 585) in which the node was not excised in one piece, and in which additional pieces were removed. These additional pieces were cut away during the experiment because it was presumed from the failure of a reduction in rate that nodal tissue must have been left behind. In No. 564, the rate fell 1.5 beats per minute (87 to 85.5) after the first piece had been removed, and 39.6 beats (85.5 to 45.9) after the excision of the second piece, a total decrease of 41.1 beats. There was stoppage of 9 seconds, but no nodal tissue was removed. In No. 569 it rose 34 beats (114 to 148) after the excision of the first piece, fell 3 beats (148 to 145) after the excision of the second, fell 31 beats (145 to 114) to the original rate, after the excision of the third piece, and only after the excision of the fourth piece was there stoppage (4.25 seconds). A portion of the node was found in this fourth piece. In No. 570 two pieces were excised: after the first had been

* See note on page 326.

removed, the rate fell 24.9 beats (118.5 to 93.6) and after the second, 8.2 beats (83.2 to 75) but there was no stoppage. Portions of the node were found in both pieces. In No. 580, after the excision of the first piece, the rate fell 0.6 beats (46.5 to 45.9); after the excision of the second, it rose 2.7 beats (45.9 to 48.6); after the excision of a third piece there was stoppage of 24 seconds. The node was found in the third piece. In No. 581, after the first excision, there was stoppage of 27.5 seconds. Subsequently the rate, as compared to the original rate, had fallen 41.1 beats (77.7 to 36.6). A higher rate (69) then set in, for the ventricles were fibrillating. A second piece was excised, and the rate fell 4.2 beats (69 to 64.8); the experiment is added here for completeness only, for it is not illustrative. In No. 583, the rate rose 19.8 beats (58.2 to 78) after the excision of the first piece, and fell 24 beats (78 to 54) to about the original rate after the excision of the second piece, while after the excision of the third piece there was stoppage. About one quarter of the node lay in piece 3. In No. 585, the rate rose 4.18 beats (54.8 to 58.98) after the excision of the first piece, and after the excision of the second, there was stoppage of 65 seconds. The second piece contained 1,410 micra of the node. It is quite clear, therefore, that excision of pieces of tissue from this region, does not by itself cause stoppage or a reduction in rate. The seven cases which have just been described and in which pieces had been excised before the node had been satisfactorily removed, maintained their rate at a speed either equal to, or above, that which was exhibited before the excisions. When, finally, a portion was excised and stoppage and slowing occurred, this piece was found to contain a large portion of the node. These seven experiments are therefore of exceptional interest and value. It is quite clear from a consideration of them, that excision of pieces of tissue from this region does not by itself cause stoppage or a reduction in rate. An exception in No. 570 will be discussed later.

Observations have also been made to determine the site of the tissue which assumes the *secondary pacemaking function* after the sino-auricular node has been excised. Auricular contraction was found to precede ventricular contraction in twenty-one experiments*; from these twenty-one, seven (577, 578, 579, 587, 588, 589 and 590)† should properly be deducted because at the time the node was excised the ventricles were already in a state of fibrillation, and only the auricles were beating co-ordinately. Ventricular contraction set the pace, preceding that of the auricles, in seven* (564, 565, 567, 571, 582, 585 and 586) experiments. In two* (557 and 560) auricle and ventricle beat practically simultaneously. Of the seven cases in which the ventricular contractions set the pace, the auricles had ceased to contract in three only. It is apparent from these facts, that after incisions or excisions in the region of the node, the auricles do not permanently cease contracting as has been claimed by Langendorff and

* See Table I.

† See Table II in the following contribution.

Lehmann,⁵ but that, on the contrary, in the majority of cases they set the pace for the ventricular contractions. It was thought at first that when the auricles set the pace for the ventricular contractions, after excision of the node, a higher rate might be developed than when the ventricular contractions had control. A study of Table I will show that this expectation is not fully realized, for the ventricles sometimes beat at a relatively high rate, as in Nos. 564, 565 and 571. But the table shows that when the auricular contractions set the pace they usually developed a higher rate than when the ventricular contractions did. On the other hand, when the ventricular contractions set the pace they may beat at a slower rate than is ever reached when the auricle is the pacemaker.

IV. Protocols of the experiments.

Experiment 557.

The heart was perfused. The rate was 114 per minute. The *S-A* node was excised, the area excised extending from the superior vena cava, wide of the sulcus terminalis, well down the wall of the auricle. The heart rate afterwards was 81.9. The auricles and ventricles beat synchronously.

Histology. The node passes through 5,000 micra. It lies to the right of the *tænia terminalis*. Its shape is that of an inverted cone. The pericardium over it is thick. It is in relation to a vessel, to nerves and ganglia. The entire node was probably excised, though a small piece of its lower end may have been left behind. Every fifth section in this series was mounted.

Experiment 558.

The heart was perfused. The rate was 121.5. The *S-A* node was excised. The excision extended from high upon the superior vena cava, almost down to the inferior vena cava. The rate afterwards was 63, and fifteen minutes later it was 58.5. The auricular preceded the ventricular contraction.

Histology. The node passes through 5,760 micra. It lies to the right of the *tænia terminalis*. Its shape is cylindrical. The pericardium over it is thick. It is in relation to vessels, nerves and ganglia. There is more than the usual amount of connective tissue. The node has been completely excised.

Experiment 559.

The heart was perfused. The rate was 99. The *S-A* node was excised. There was complete cessation of the heart beat for about 30 seconds. The subsequent rate was 36. At first the ventricle set the pace for the auricular contractions, then the ventricular and auricular contractions were synchronous, while later the ventricular preceded the auricular contractions. Five minutes later the auricular preceded the ventricular contractions. The rate was 33.9 per minute, later it became 32.7.

Histology. The node passes through 7,830 micra. It lies to the right of the *tænia terminalis*. At the lower level, it lies slightly more toward the atrium. The vessel is found in the lower part only. There are only a few ganglion cells. The pericardium is not thick. The node has been completely excised.

Experiment 560.

The heart was perfused. The rate was 81. The area of the *S-A* node was excised, when the whole heart ceased to beat for a period of from 20 to 30 seconds. At first the rate was 18.75. The auricles and ventricles beat synchronously, the rate later being 27.75. Then the ventricular preceded the auricular contractions by 0.08 seconds, the rate being 31.8.

Histology. The node passes through 5,520 micra. It is in relation to a vessel, nerves and ganglia. The pericardium over the node is thick. Its shape is that of an inverted cone. The node has been entirely excised.

Experiment 561.

The heart was perfused. The rate was 90. The area of the *S-A* node was excised in two stages. Incisions 1, 2 and 3 were made, after which the rate was 123. Incision 4 was then made,

thus completing the excision of the node. There was cessation of the heart beat for 4 seconds. The subsequent rate was 21, the auricular contractions preceding the ventricular by 0.12 seconds. The rate then rose to 39, and 5 minutes later to 51: finally, 22 minutes later, it dropped to 45.

Histology. The node passes through 4,330 micra. It lies to the right of the tænia terminalis. Its shape is that of an inverted cone. The pericardium over it is thin. The vessels in relation to it are small and present in the lower levels only. There are but few nerves and ganglia. A considerable amount of nodal tissue was left at the top and a small amount below. The node had not been excised completely.

Experiment 562.

The heart was perfused. The rate was 57.9. Incisions 1, 2 and 3 were made, after which the rate rose to 63. Incision 4 was then made, completing the excision of the node bearing area. The rate rose to 88.5. There was no stoppage. The rate subsequently dropped to 72. The auricular preceded the ventricular contractions.



Histology. The node passes through 6,040 micra. There is nodal tissue remaining above* and also below to the right (Fig. 2). The pericardium is thick. The node lies in relation to ganglia and to a small vessel at the lower extremity only. The shaded portion in the figure indicates the position of the S-A node.

Experiment 563.

The heart was perfused. The rate was 88.5. Incisions 1, 2 and 3 were made, when the rate rose to 96.9. After incision 4, excision of the node-bearing area was completed and the rate fell to 63.9. The rate later rose to 79.5. Six minutes later, it fell to 65.5, while seven minutes later it rose again to 84.9. There was no stoppage. The auricular contractions preceded the ventricular.

Histology. The node passes through 2,990 micra. A considerable portion of the top is left behind. Some of the node also remains below. It lies beneath the right portion of the tænia terminalis. The pericardium is thick. It is in relation to a vessel and a few ganglion cells.

Experiment 564.

The heart was perfused. The rate was 87 and ten minutes later it was 86.25. Incisions 1, 2 and 3 were made (1 in Fig. 3) and then the rate rose to 93. After incision 4 (2 in Fig. 3) the rate fell to 85.5. There was no stoppage. A pair of parallel incisions (3 in Fig. 3) were then made. One, that to the right, ran at a slight angle to the sulcus terminalis. There was stoppage of the whole heart for 9 seconds, after which the ventricular set the pace for the auricular contractions. Twenty-four such contractions occurred in 33.75 seconds. Then, after the cessation of the whole heart for 12 seconds, the rate was 18.9. The excision (incision 4 in Fig. 3) of the second piece was then completed. The rate was 28.5. The auricular and ventricular contractions were synchronous. Later the ventricular preceded the auricular contractions by 0.12 seconds. The rate was finally 45.9.

Histology. In neither of the pieces excised, can nodal tissue be seen. The rest of the auricle left behind was cut in series. The node was identified in this through 1,840 micra, beginning high in the antero-left wall of the superior vena cava. The node is in relation to a vessel, nerves and ganglia. The situation of the node in reference to the excised area is seen in Fig. 4.

* The drawing does not indicate this relation; the nodal tissue should have been drawn to cross line 1.



Fig. 3.

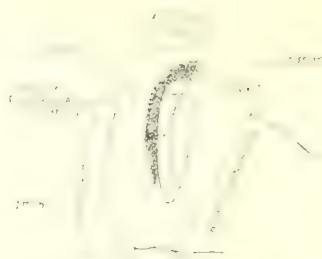


Fig. 4.

Experiment 565.

The heart was perfused. The rate was 93; sixteen minutes later it was 70.5. The usual incisions 1, 2 and 3 were made, after which the rate rose to 120.9; one minute later it was 93. Incision 4 was then made, and the heart stopped for 25.7 seconds. After this the ventricular preceded the auricular contractions by 0.1 seconds and the rate was 24.9. Between the first and second systoles after stoppage there was an interval of 9.25 seconds; between the second and third, 6 seconds; between the third and fourth, 4.3 seconds; between the fourth and fifth, 3.5 seconds. Fifteen minutes later, the rate was 36.9 and the *Vs-As* interval 0.1 to 0.2 seconds. The rate was 33, and 34 minutes later 27.5.

Histology. The node passes through 4,350 micra. It is in relation to a small vessel, ganglia and nerves. The node was entirely excised. The node lies to the right of the *tænia terminalis*.

Experiment 567.

Thirteen minutes after the heart was suspended, the ventricles began to fibrillate. Twenty c.c. of a 1 per cent. potassium iodide solution were injected, after which the heart beat co-ordinatedly and regularly, the rate being 68.25. Incisions 1, 2 and 3 were made and the rate increased to 93. After the fourth incision, the heart stopped for 10.2 seconds and the rate then fell to 6.9. Between the first and second contractions there was a pause of 27.25 seconds; between the second and third, one of about 25 seconds; between the third and fourth one of 50.25 seconds. At first the auricles and ventricles beat synchronously, later the ventricular preceded the auricular contractions. Later still (fourteen minutes after the fourth incision) the auricles ceased to beat. The rate, twenty-five minutes after the fourth incision, rose to 29.25; the experiment was then stopped.

Histology. The node passes through 5,550 micra. The pericardium over the lower levels of it is thick. The node is in relation to nerves and a vessel. A portion of it remains at the top and probably a slight amount below. It lies between and stretches from the pericardium to the endocardium, just a little to the right of the *tænia terminalis*. In some parts it is triangular, and in others saddle shaped, the saddle fitting over the *tænia*, viewed in cross-section.

Experiment 569.

The heart was perfused. The rate was 118.5, then 114. Incisions 1, 2, 3 and 4 were made, when the rate rose to 148. There was no stoppage after the excision of the first piece. A second piece was excised (Fig. 5) after which the rate was 145. A third piece was excised from the



Fig. 5

anterior portion of the superior vena cava, when the rate fell to 114. A fourth piece was excised at the angle of junction of the superior vena cava and the right auricular appendix. Then there

was immediate stoppage for 4.25 seconds. The rate was 66, the ventricular setting the pace for the auricular contractions. Between the first and second contractions after stoppage there was a pause of 4.25 seconds; between the second and third, of 10.75 seconds; between the third and fourth, of 5 seconds; between the fourth and fifth, of 3 seconds; between the fifth and sixth, of 2.3 seconds. Two and a half minutes later the rate was 52.5. Auricular now preceded ventricular contraction, the A-S interval being 0.1 seconds. Finally the rate was 31.8.

Histology. Piece 1. The node passes through 3,600 micra; very little superfluous tissue is removed. It lies to the right of the *tænia terminalis*. Its general shape is that of an inverted cone, but its apex lies nearer the endo- than the pericardium. The middle portions are flatter, the upper portions more circular. It lies in relation to a vessel, nerves and ganglia. Piece 2 was not examined. Piece 3 contains no nodal tissue. Piece 4. The node passes through 300 micra; it is completely excised.

Experiment 570.

The heart was perfused. The rate was 118.5 and later 106.5. The node was excised by incisions 1, 2, 3 and 4 (1 in Fig. 6). Afterwards the rate fell to 93.6 and then to 83.25. There was no stoppage. A second (2 in Fig. 6) piece was excised. Stoppage did not occur, though the rate fell to 75.



Fig. 6.

Histology. The node passes through 8,760 micra. The pericardium is thick. It lies to the right of the *tænia terminalis*. The shape of the node is that of an inverted cone. It is in relation to a vessel and to nerves. It is found in those portions of both pieces which are adjacent to each other. At the upper part of piece 2, nodal tissue is seen and is well developed. Here a considerable amount of nodal tissue may have been left behind. The entire node has probably not been excised.

Comment: The absence of stoppage after the excision of both pieces was due to the fact that a large portion of the node had probably been left behind.

Experiment 571.

The heart was perfused. The rate was 96. The auricles were not contracting. A moderately wide excision of the S-A node was made in one stage. Though the auricles could not be seen to contract, the ventricles stopped for 7.5 seconds. The rate after the excision was 23.25, then rose to 32.25, and later to 33.9. Interpolated ventricular extrasystoles were produced by induction shocks; it is likely, although auricular contractions were not seen, that the auricles may still have been setting the pace.

Histology. The node passes through 4,250 micra. It lies to the right of the *tænia terminalis* and is somewhat saddle shaped in cross section. The pericardium over the node is thick. It is in relation to a vessel, but there are no nerves and ganglia to be seen. The node was incompletely excised. A considerable amount of nodal tissue was left in below.

Experiment 572.

The heart was perfused. The rate was 82.5. After incisions 1, 2 and 3, the rate rose to 111. After excision there was stoppage for 92 seconds. After this the rate varied between 42 and 22. The auricular preceded the ventricular contractions; later the auricles ceased to register their contractions but these could be seen and were indicated by pencil marks on the curve; there was A-V dissociation, 22:6:9.

Histology. The node passes through 5,350 micra. It lies to the right of the *tænia terminalis*. Its shape is that of an inverted cone. The pericardium over it, and the connective tissue through it, are both thicker than usual. It is in relation to a vessel, nerves and ganglia. The node has been completely excised, and the least possible auricular tissue has been removed with it.

Experiment 575.

The heart was perfused. The rate was 60.6. After incision 1, 2 and 3 the rate rose to 64.5. After excision of the S-A node there was stoppage of the auricles for 4 seconds, and the ventricles fibrillated immediately. There was now a complete auricular irregularity, the rate being 47.4. The A-V bundle was then cut, and the auricles beat regularly, their rate being 19.8.* It is interesting to note in this and in other experiments where the ventricles were fibrillating that the auricles certainly continued to contract (see Langendorff and Lehmann).

Histology. The node passes through 5,740 micra. It is an inverted cone and is in relation to a vessel and to nerves. The node was completely excised. The A-V bundle is divided.

Experiment 576.

The heart was perfused. The rate was 51 and later 83.4. After the third incision the rate was 92.4. After the fourth incision there was stoppage for 117.5 seconds (Fig. 7). The auricles

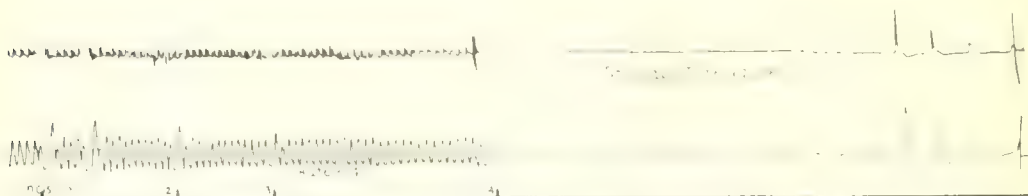


FIG. 7. *Experiment 576.* Shows excision of the S-A node. Incisions 1, 2 and 3 with stoppage after incision 4 are shown. There is stoppage of 117.5 seconds. The return of the auricular and ventricular contractions are seen at the end of the curve. The dotted lines in this and in succeeding curves indicate that portions of the curves, during which no contractions of the heart occurred, have been omitted.

and ventricles then began to beat again, the auricular preceding the ventricular contractions at the rate of 22.5 and then 23.1. Ventricular fibrillation was induced by faradization. The auricular rhythm was completely irregular, the rate being 36.9. The A-V bundle was then cut and after a few contractions, the auricles ceased to beat. Two and a half minutes later they began to beat regularly, the rate being 21.6 and later 24.9. After a rise in the pressure (30 to 45 mm.) the auricles contracted irregularly, the rate being at first unchanged but later rose to 57. The rate fell again to 35.4 and 36.3 while the rhythm remained regular.

Histology. The S-A node measured 2,270 micra. It is an inverted cone. It is in relation with a vessel, nerves and ganglia. A small part was probably left in above. The A-V incision lies far behind the A-V node so that the auriculo-nodal junction instead of the A-V bundle is divided, but the division is not complete (Fig. 8).

FIG. 8.

* The bearing of experiments in this group will be spoken of later. It may be mentioned briefly here that fibrillation of the ventricles brings about a rhythm in the auricles, directly comparable to that in the ventricles when the auricles are fibrillating. These facts are used to illustrate certain functions of the A-V bundle and of the S-A node.

Comment : The rise in pressure, noted above, no doubt restored the few fibres of the auriculo-nodal junction to temporary functional activity only, so that the auricles responded to ventricular fibrillation. Later the A-V bundle failed to act and the auricular rhythm again became regular.

Experiment 577.

The heart was perfused. The rate of the auricles was 60. Ventricular fibrillation was induced by faradization. There was complete auricular irregularity, the rate being 66. Three minutes later the auricles beat regularly, at the rate of 54. Incisions 1, 2 and 3 were then made in the region of the S-A node; the rate rose to 59 and the rhythm was still regular. Incision 4 was then made. There was no stoppage, but the rate fell to 34.4 and auricular irregularity reappeared. The A-V bundle was then incised, approximately 1 mm. anterior to the anterior lip of the coronary sinus; the auricles remained irregular. This unexpected result induced us to make a second incision of the A-V bundle, 3 mm. anterior to the first one, after which three irregular contractions followed, and then the auricles ceased beating.

Histology. The S-A node passes through 7,440 micra. Nodal tissue was left behind, both above and below. The A-V bundle is only partially cut through.

Comment : A probable interpretation of the events in this experiment is as follows : the sinus node after a primary failure, maintained auricular regularity. After excision of the sinus, the auricle responded to the fibrillating ventricle. Whether or not the auricular contractions would have remained irregular after incision of the A-V bundle is problematic. The bundle was not completely divided, as the serial sections show.

Experiment 578.

The heart was perfused. The rate of the heart was 79.8 and the rhythm was regular. Ventricular fibrillation was then induced by faradization. The auricular contractions remained regular at a rate of 79.2. Incisions 1, 2 and 3 were made, and the rate rose to 98.4; the rhythm was still regular. Incision 4 was then made and the auricles ceased beating for 50 seconds. The second auricular systole occurred 8.5 seconds after the first. The auricular rate fell to 19.4 and was completely irregular. Later the rate was 19.8, then 16.2, then 20.8 and finally 24.6. The A-V bundle was not cut.

Histology. The S-A node passes through 3,320 micra and is in relation to a vessel, nerves and ganglia. It had been thought that a slight amount had been left behind both above and below, but examination of those portions fails to show nodal tissue.

Experiment 579.

The heart was perfused *in situ*. Ventricular fibrillation was induced by faradization. The rate of the auricles was 60 and the rhythm practically regular. The S-A node was excised by incisions 4, 3 and 2 only. The auricular contractions stopped for 19 seconds and then became more rapid and quite irregular. They became regular later, the rate being 51.75 and remained so for 15 minutes, when perfusion was stopped.

Histology. In the piece excised the node passes through 2,250 micra. It is thin and lies under the pericardium. The portion of the node left behind passes through 1,020 micra, and is well developed. A large vessel has been cut across. It lies in relation with a vessel, nerves and ganglia.

Comment : The rhythm of the auricles after fibrillation, and before the excision of the S-A node, was very slightly irregular, the irregularity probably being only apparent and due to instrumental error. Successive groups of five beats occupied equal time. After the excision of the sinus bearing area, a complete irregularity set in which lasted seven minutes. The auricular contractions then resumed a completely regular rhythm and this was maintained until the end of the experiment. The curve does not permit a statement as to whether this change took place suddenly or gradually. The return to regular rhythm is explained by the fact that there was an incomplete excision of the node, one third of the entire structure having been left behind. A return of the function of this area determined the subsequent regularity of the auricles.

Experiment 580.

The heart was perfused *in situ*. The rate of the heart was 46.5. Incisions 1, 2 and 3 (in Fig. 9), were made and the rate rose to 56.4. After incision 4 there was no stoppage, but the rate fell to 45.9. A second piece (2 in Fig. 9), was then excised; there was no stoppage and the rate rose to 48.6. A third piece was then excised (3 in Fig. 9), whereupon the heart contracted a few times and stopped for 24 seconds. The auricular preceded the ventricular contractions. The second beat occurred after 22.7 seconds, the third beat after 10.1 seconds. The rhythm of the heart was slightly irregular, but became regular again at the rate of 39.3. Later the ventricular preceded the auricular contractions, the rate being 14.7. Ventricular fibrillation was then induced by faradization. The auricular rhythm became completely irregular, the rate rose to 41.4, continued so for 10 minutes and then the auricles ceased to beat.

Histology. In pieces 1 and 2, no nodal tissue was seen. In piece 3, the node passes through 3,200 micra. It is in relation to a vessel, a few nerves and ganglia. At the lower portion of piece 3, a portion of the node seems to have been left behind. The adjacent portion of the auricle was cut in series and examined, but nodal tissue was not identified.

Comment: This experiment is interesting for the same reason as No. 569. In both, multiple incisions and excisions in the neighbourhood of the node were performed without important changes in the rhythm of the heart. Only the excision of the node-bearing area brought about stoppage and the attendant phenomena.



Fig. 9.



Fig. 10.

Experiment 581.

The heart was perfused *in situ*. The rate was 77.7. After incisions 1, 2 and 3 were made the rate increased to 89.4. Incision 4 was then made and there was stoppage for 27.5 seconds, auricular preceding ventricular contractions. The second beat came 29 seconds later. The rate gradually rose to 36.6. Ventricular fibrillation was then induced. The auricles beat regularly at a rate of 69. A second piece of auricular tissue was next excised and the rate fell to 64.8, but the rhythm was still regular. The ventricles were again faradized and the rate rose to 69.6. Finally the ventricles were again faradized and a very slight irregularity occurred in the auricular rhythm.

Histology. The node is somewhat flattened from side to side throughout. It passes through 3,420 micra in the lower piece (1, Fig. 10). The pericardium over the node is thin, there are very few ganglion cells in relation with it, but there is a large vessel. Possibly a small amount of nodal tissue is to be found in the lower portion of piece 2 (Fig. 10). The remainder of the auricle was cut in serial sections and in it nodal tissue was found (400 micra).

Comment: The failure of ventricular fibrillation to induce auricular irregularity was probably due to the portion of nodal tissue which had been left behind. This piece maintained the usual auricular rhythm.

Experiment 582.

The heart was perfused *in situ*. The rate was 57.2. After incisions 1, 2 and 3 had been made the rate rose to 65.1. Incision 4 was made and the heart stopped for 37.5 seconds. The auricular preceded the ventricular contractions. Then the auricles ceased and the ventricular rate fell to 17.35. Faradization of the ventricles failed to result in fibrillation and spontaneous ventricular contractions began after it ceased. The ventricles were faradized again and fibrillation set in and continued to the end of the experiment.

Histology. The node passes through 1,750 micra. It is cylindrical from top to bottom. Portions at both extremities were probably left behind. There are nerves, vessels and ganglia in relation to the node. There is unusual development of connective tissue.

Experiment 583.

The heart was perfused *in situ*. The rate was 58.2. Incisions 1, 2 and 3 were made and the rate rose to 61.6. Incision 4 was then made (1 in Fig. 11). There was no stoppage of the heart and the rate rose to 78. Then a second piece (2 in Fig. 11) was excised; there was no stoppage, but the rate dropped to 54. Fibrillation of the ventricles was induced by faradization, but the auricular rhythm remained perfectly regular. Then a third piece (3 in Fig. 11) was excised, the heart stopped for 29.75 seconds and a rate of 26.4 developed. There was complete auricular irregularity, the rate being fast at first and later slow. The A-V bundle was then cut. After this procedure a few auricular systoles occurred at long intervals. Rhythmic stimulation of the auricles was ineffectual in causing them to contract. The experiment was stopped.

Fig. 11.

Histology. The node passes through 4,800 micra of piece 1, through 2,230 micra of piece 2, and through 2,190 micra of piece 3, making a total of 9,220 micra. A small amount of nodal tissue was probably left behind, at the very top of piece 2. The node lies in relation to a vessel. There are many nerves and ganglia.

Comment: The experiment should be compared with Nos. 569 and 580. The functions of the node are well illustrated; it is unfortunate that the auricles ceased to contract after the A-V bundle was cut.

Experiment 584.

The heart was perfused *in situ*. The rate was 51.9. Incisions 1, 2 and 3 were made and the rate rose to 54.5. Later it fell to 42. Incision 4 was then made (Fig. 12), and the rate fell further to 39.4. Fibrillation of the ventricles was then induced by faradization (Fig. 13). The auricular contractions remained regular at a rate of 51.6. An incision was then made parallel to the *tænia terminalis*, but to the left of it, reaching almost to the level of the A-V groove. Before the incision the auricular rate was 58.2; after, it fell to 37.5 and complete auricular irregularity set in (Fig. 14). After a few slow contractions the auricles stopped for 37.2 seconds, and an irregular auricular rhythm at a rate of 11.9 set in. The A-V bundle was cut (Fig. 15) and then the auricles ceased to beat for 14 seconds, but later beat at a regular rhythm, first of 25.5 and later of 28.5, 31.2, and 33.6. The pressure of the perfusion fluid had fallen to zero but was raised to 30 mm. The experiment was stopped on account of inadequate perfusion.

Histology. The node passes through 5,730 micra. The shape is that of an inverted cone. A portion is left in at the upper extremity. Sections of the portion left behind show the presence of the node through 1,520 micra on the left anterior portion of the superior vena cava.

Comment: The area excised contained about five-sevenths of the node, but the portion excised was insufficient to produce stoppage and slowing, for two-sevenths of the node had been left behind. Consequently when ventricular fibrillation was induced, the auricular rate remained regular and so continued until an incision to the A-V groove had been made in the auricle. Then the auricles ceased to beat for a time, but later contracted again in a completely irregular rhythm. When the A-V bundle was cut, the auricles became regular. It is difficult to understand why the portion of the node left behind was incapable of maintaining a regular auricular rhythm, after the final incision to the A-V groove had been made. It did maintain regular auricular contractions after ventricular fibrillation had been induced, and remained efficient until this incision had been made. This experiment is discussed again later.

Experiment 585.

The heart was perfused *in situ*. The rate was 54.8. The area bearing the S-A node was excised in two pieces. The rate after incision 3 rose to 58.98 (Fig. 16). The rate before the excision of the second piece was 51. A stoppage of 65 seconds occurred (Fig. 17) after the second piece was excised. The ventricular preceded the auricular contractions. About two to three minutes after stoppage the rate dropped to 10.2 but later rose to 14.75 (Fig. 18).

Histology. In piece 1 the node passes through 5,660 micra; a portion is left behind at the top. The node is wedge shaped, and stretches from endo- to pericardium. In piece 2, it extends through 1,410 micra. The portion identified as node has a somewhat uncertain histology. The node lies to the right of the *tænia*. It is in relation to a vessel and also to ganglia.

Experiment 586.

The heart was perfused *in situ*. The rate was 60.6. Incision 1 (Fig. 19) was made. No stoppage occurred, but conspicuous slowing to 21.9, the auricular preceding the ventricular contractions. Then incisions 2, 3 and 4 were made and were followed by no perceptible change in rate. Incision

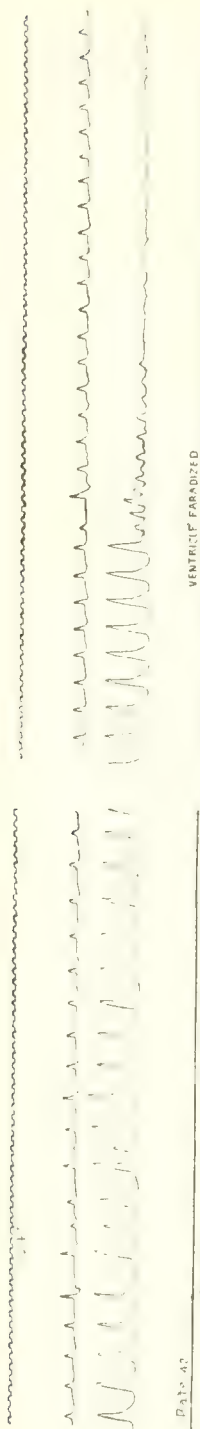


Fig. 12. Experiment 584. Shows incision 4, after which there are slight irregularities in the rhythm of the whole heart, but no stoppage.

VENTRICLE PARALYZED

Fig. 13 shows faradization resulting in fibrillation of the ventricle, but without change in the auricular rhythm. There is a slight acceleration of the rate.

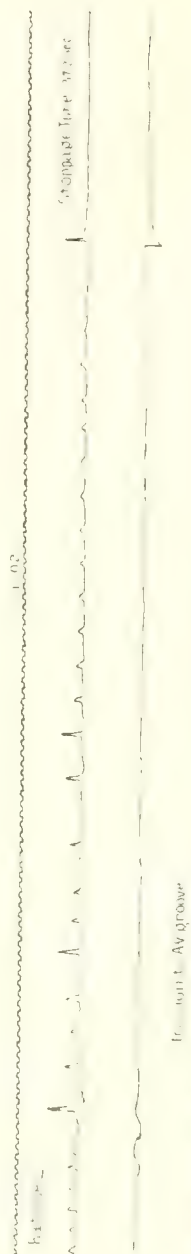


Fig. 14. Incision 5 is shown at the beginning of the curve. Shortly afterward there is stoppage of 37.2 seconds.

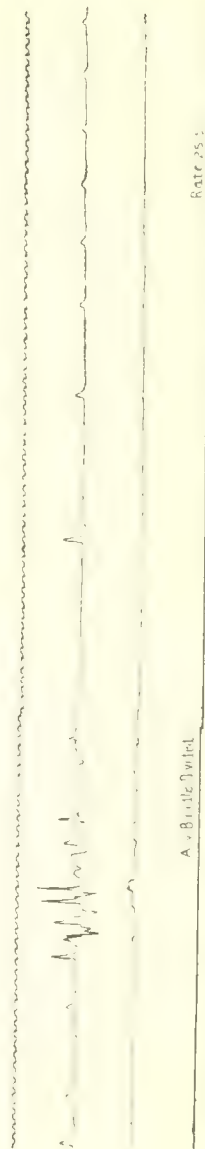


Fig. 15. Shows the division of the A-V bundle. After the division the rhythm of the auricles is regular and the rate is 25.5.

5 was made parallel to the terna terminalis and downward to the A-I' groove. The rate rose from 21.9 to 75 during 19 seconds, and then the heart stopped for 20.5 seconds. The first was followed by a second pause of 26 seconds, a third by 11 seconds, and a fourth by 53.5 seconds. The rate became gradually faster rising to 15.6, the ventricular preceding the auricular contractions. The ventricles were faradized but fibrillation did not ensue. Later fibrillation occurred, accompanied by complete irregularity of the auricles. At the end of faradization, a regular

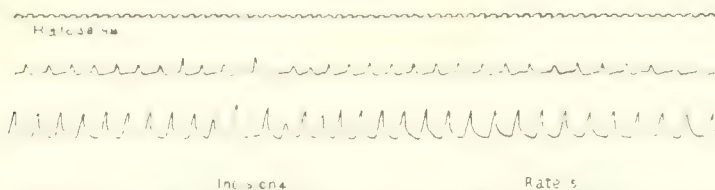


Fig. 16. *Experiment 585.* Curve showing excision of the first piece of auricular tissue. There is no stoppage.

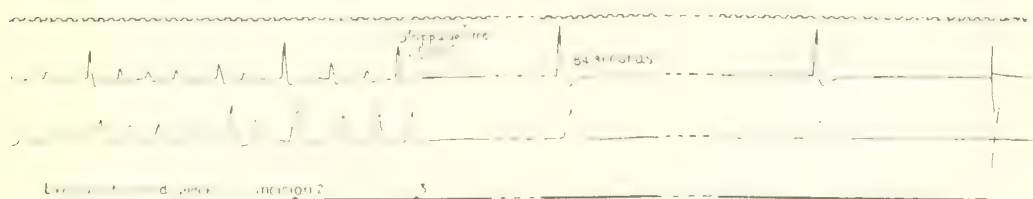


Fig. 17. *Experiment 585.* Excision of the second piece of auricular tissue is shown. There is stoppage of 65 seconds. Between the first and second contractions there is a pause of 84 seconds.

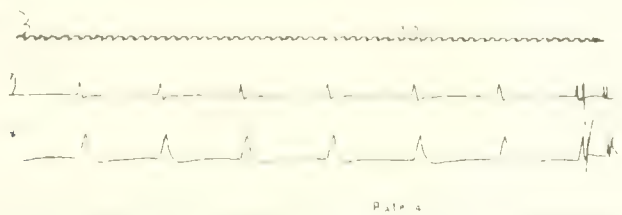


Fig. 18. *Experiment 585.* The rate after excision of second piece is 14.7. The ventricular precede the auricular contractions.

ventricular rhythm returned. Faradization of the auricular muscle was accompanied by complete irregularity of the ventricles. The ventricles were faradized again, fibrillation took place and this together with complete auricular irregularity persisted till the end of the experiment. The A-V bundle was cut, but a cusp of the aortic valve was incised, causing a fall of pressure in the circulating fluid, and bringing the experiment to an end. The auricles afterwards beat regularly for eight contractions.



Fig. 19

Histology. The node passes through 7,800 micra. It lies to the right of the tania terminatis. A slight amount is probably left in below. In cross section it is circular. It is in relation to ganglia and small vessels. Sections through the superior vena cava and auricle left behind show that the node passes through 1,600 micra, in the superior vena cava.

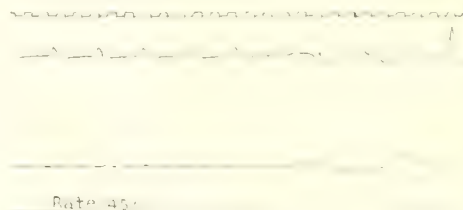
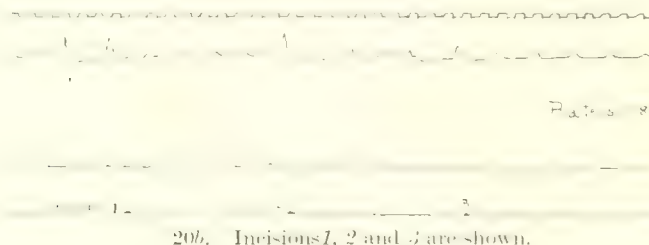
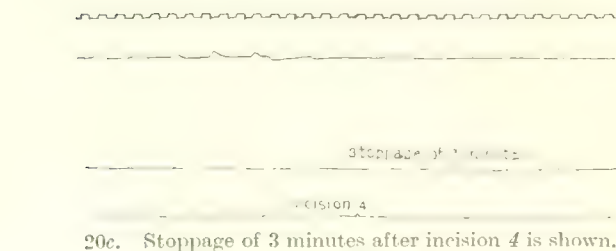


Fig. 20a. Experiment 589. The ventricle is fibrillating. A regular auricular rhythm is seen.



20b. Incisions 1, 2 and 3 are shown.



20c. Stoppage of 3 minutes after incision 4 is shown.

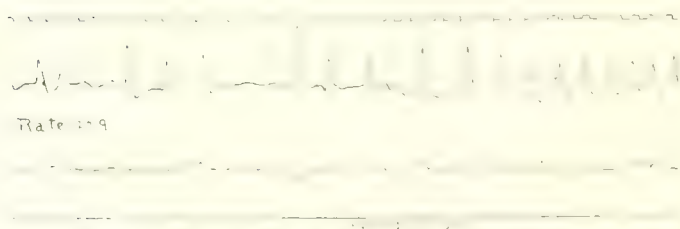


Fig. 21a. Experiment 589. The first part shows a complete irregularity of the auricle and the division of the A-V bundle is shown.

Experiment 587.

The heart was perfused *in situ*. Spontaneous fibrillation of the ventricles accompanied by complete auricular irregularity set in. The auricular rate varied from 87 to 99. The A-V bundle was incised and the rate of the auricular contractions fell to 76.2, but the rhythm of the auricles was not quite regular. A second incision of the A-V bundle was therefore made. The auricular rhythm became regular at the rate of 85.2, and a little later 86.1. The S-A node was excised, incisions 1, 2 and 3 being made. The rate after the third incision rose to 92.28. After incision 4 there was stoppage for 6.6 seconds. The rate gradually rose to 44.1 and the rhythm was regular

Histology. The node is completely excised. It passes through 5,200 micra. It is in relation to a vessel, ganglia and nerves, the latter being seen more especially at the lower levels. The node lies to the right of the tænia terminalis.

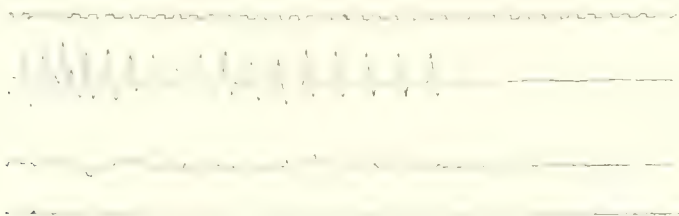
Experiment 588.

The heart was perfused *in situ*. The ventricles fibrillated spontaneously. The auricular rate was 50.1, and regular. The S-A node was excised. After the incision 3 the rate was 50.72. After incision 4 there was stoppage for 17.5 seconds and between the first and second beats for 161 seconds. The auricular rhythm was completely irregular and the rate was 53.25.

Histology. The node passes through 3,310 micra. A small amount is left in at the top towards the right. The node is in relation to ganglia and to a vessel. The nodal tissue is peculiar in that the cells are somewhat vacuolated, resembling the Purkinje type. They are stained much lighter than the surrounding tissue. Towards the upper end of the node the tissue becomes more compact, and approaches more nearly to the usual appearance of the node, but still retains its somewhat vacuolated appearance.

Experiment 589.

The heart was perfused *in situ*. Fibrillation of the ventricles was induced by faradization. The auricular rate was 45.6 and the rhythm was regular (Fig. 20a). The S-A node was excised.



21b. Stoppage of auricular contraction subsequent to the division of the bundle is shown.

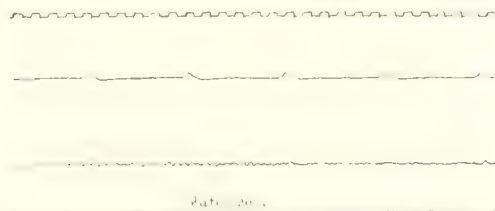


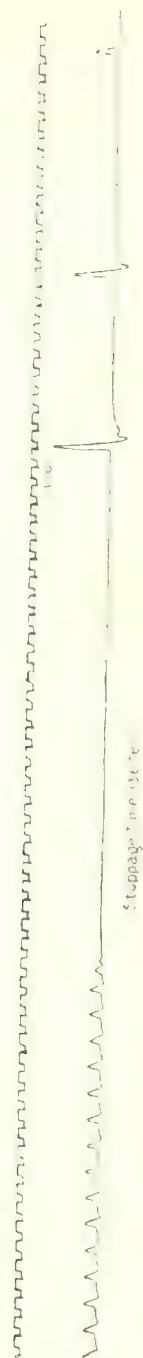
Fig. 22. *Experiment 589.* Shows a regular auricular rhythm after the division of the A-V bundle. The rate is 20.62.

The rate after incision 3 was 55.08. (Fig. 20b). After incision 4, there was stoppage for three minutes. (Fig. 20c). The anterior coronary artery was tied off. The auricular rate gradually rose to 27.9 and the rhythm was completely irregular. The A-V bundle was cut and the auricular contractions were regular (Fig. 21a). After a few beats the auricles ceased to contract (Fig. 21b). During the cutting of the bundle, a semi lunar valve was incised; this accident unfortunately brought the experiment to an end. At the end the auricular rate was 20.62 (Fig. 22), and the rhythm was regular.

Histology. The node passes through 5,290 micra. It is in relation to vessels and ganglia. The pericardium is not thick. A small amount of nodal tissue is probably left in below.

Experiment 590.

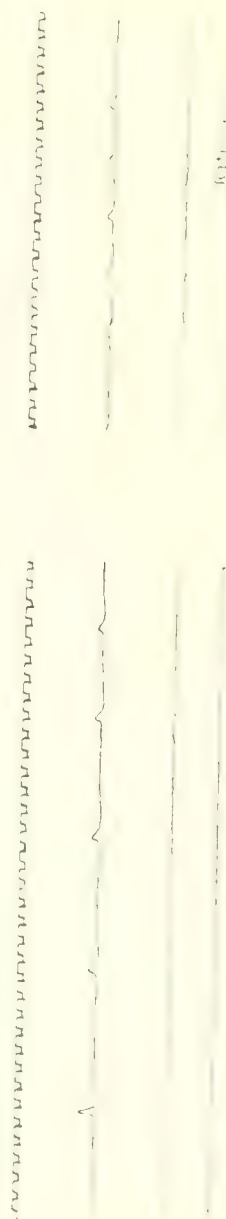
The heart was perfused *in situ*. Fibrillation of the ventricles was induced by faradization. Complete auricular irregularity followed. The rate was 96.9. Occasionally there was a tendency for the auricles to beat regularly, so the S-A node was stimulated rhythmically by single induction shocks to increase the irritability of the node, and to restore it to its function of maintaining the



Rate 800

1 2 3 4

Fig. 23a. Experiment 599. Fraction 4 completing excision of the S 4 node is seen. There is stoppage of 13.6 γ and λ .



23b. Shows the annular rate gradually increasing.

23c. This curve is taken later and shows the annular confining at a rate of 29.

auricular contractions. This procedure made the auricular rhythm regular for a short time but the irregularity recurred. This method of stimulation was repeated three times, on each occasion with the same result. The 4-4 bundle was then cut. The auricular rhythm became regular, the rate being 79.2 and the S: A ratio 82:8. The S: A node was excised (Fig. 23*a*). Auricular contractions stopped for 13.6 seconds. The rate later was 39 and the rhythm then remained regular (Fig. 23*c*).

Histology. The node passes through 2,250 micra. It is in relation to a vessel, nerves and ganglia. A small amount of nodal tissue is left in at the top. The general shape of the node is cylindrical.

V. Discussion of the variant experiments.

It will be found convenient to discuss Experiments 564, 584 and 586 together. In Experiment 564, incision 3 (Fig. 3) crossed the *tænia terminalis* and the heart stopped before the node bearing area had been removed. The final incision produced no effect. In Experiment 584, the auricular rhythm remained regular after a portion supposed to contain the S-A node had been removed, although the ventricles were fibrillating. The regularity of the auricular contractions indicated that a portion of the S-A node must have been left behind, for the maintenance of regularity is a function which resides in the node under experimental conditions. It was decided to remove an additional piece of tissue. An incision (Fig. 19) was made, parallel with the sulcus terminalis, which reached almost to the A-V groove. After a few slow contractions, the auricular contractions stopped for 37.2 seconds. The rhythm was then irregular and the rate was 19.8. The stoppage, the reduction in rate and the onset of an irregular rhythm would under ordinary circumstances indicate that the sino-auricular node had been excised. Here, however, a mere incision caused these events. Experiment 586 is a duplicate of Experiment 584. Beside the facts mentioned an additional one must be noted as common to these three experiments. The stoppage which occurred after the single incision in Experiment 564 did not take place immediately, as is the rule, but after 24 contractions, following a primary pause of 9 seconds, the stoppage time being 33.75 seconds; in Experiment 584 after a few slow contractions there was a subsequent stoppage of 37.2 seconds; and in Experiment 586 after beating at a rate of 75 contractions for 19 seconds, the heart stopped for 20.5 seconds. That is to say, in each of these three a number of contractions occurred before the contractions stopped, an occurrence which took place in no other experiments. The histological facts in these experiments are as follows: in Experiment 564, nodal tissue (1,840 micra) was only seen in the piece left behind; in Experiment 584, 5,730 micra of the node were removed, while 1,520 were left behind (*i.e.*, 21 per cent. was left behind); in Experiment 586, 7,800 micra of nodal tissue were removed while 1,600 micra of the node were left behind, some of it above and some below. Histologically, therefore, the three cases have in common the fact that a considerable amount of nodal tissue was left behind.

In explanation of these cases, we might suppose the simple incision cut across a single muscular tract leading from the sino-auricular node in the sense of Thorel.¹⁶ But careful search for such fibres, in the serial sections,

failed to find such a tract in the auricles upon which Experiments 564 and 584 were performed. Other hypotheses to explain the events here narrated, are also unsatisfactory. Except for the fact that they occurred under circumstances quite different from those in Hering's experiments, they belong to a group where simple incision produced profound results. The amount of trauma, the circulatory disturbances and the fact that the incision increased the isolation of that portion of the node left behind after some temporary irritation is the only explanation that is justified, although it is incomplete. Anomalous events, such as the decrease in rate after incision 3, in Experiment 586 cannot be explained. We leave the matter with the report of these three experiments, in which similar experimental phenomena took place: in which an incision toward the *A-V* groove was made; and in which a large portion of the sino-auricular node had been removed.

Experiment 577 is included among the experiments in which the sino-auricular node was almost completely excised, because, after the excision of the tissue, the auricular rate fell, and because the rhythm became disordered, after the onset of ventricular fibrillation. The maintenance of a regular auricular rhythm by the sino-auricular node, in the presence of ventricular fibrillation, is considered to be one of the functions of this structure in the perfused heart. The contraction of the heart should have stopped, but seeing that the impulses from the fibrillating ventricles were already impinging on auricular tissue when the sino-auricular node was excised, stoppage need not have been a necessary consequence though it usually occurred under similar circumstances elsewhere.

Experiment 588 is mentioned for comment, because after stoppage of the heart for 17.5 seconds, the rate rose (50.1 to 53.25) instead of falling. Except that the ventricles were fibrillating at the time, and that impulses from them must have been conveyed to the auricles, there is no explanation for the increase.

CONCLUSIONS.

A series of experiments is presented in which the functions of the sino-auricular node were investigated by means of excision of the node bearing area in the perfused dog's heart. The success or failure of the excision was verified by the microscopic examination of the excised portions. Based on by far the greater number of cases, the conclusion that the sino-auricular node is the pacemaker of the heart is arrived at for the following reasons.

1. Incisions, single or multiple, in the region of the sinus node serve merely to accelerate the speed of the whole heart.

2. An excision of the sinus node (demonstrated to be successful in the examination of the histological series) results in an immediate cessation of the contractions of the whole heart. Excision of neighbouring portions fails to produce any of the results that excision of the node itself produces.

3. After excision of the sinus node, the rate of the whole heart falls and does not again reach the original rate.

4. The function of the secondary pacemaker devolves on no special portion of the heart. Sometimes a portion of the auricles, sometimes a portion of the ventricles, and sometimes a portion lying between them (as indicated by a reduction in the *As-Vs* time) takes up the function of the excised node.

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of p	Rate before adjustment	Rate after adjustment
7	114	
8	121.5	
9	99	
0	82.5	
1	90	123
2	57.9	63
3	88.5	96
4	87	93
5	70.5	120
6	68.2	94
7	114	118
8	118.5	93
9	96	0.00
0	85.2	114
1	60.6	64
2	83.4	92
3	54	59
4	79.2	48
5	60	3.00
6	46.5	36
7	77.7	89
8	57.2	65
9	58.2	61
0	51.9	54
1	54.8	58
2	60.6	21
3	86.1	92
4	56.4	50
5	45.6	55
6	82.8	83

* Rate after stock

† U's signifies the

* U's lib. signifies

TABLE I.

[illegible][illegible]

FURTHER OBSERVATIONS ON THE FUNCTION OF THE SINO-AURICULAR NODE.

(*An Appendix to the last paper.*)

BY ALFRED E. COHN AND HOWARD H. MASON.

(*From the Department of Pathology, College of Physicians and Surgeons,
Columbia University, New York.*)

It has been established by Lewis¹ and Rothberger and Winterberg², following the original observations by Cushman and Edmunds¹ and by Fredericq,² that fibrillation of the auricles is accompanied by complete irregularity of the ventricles. The reverse condition has been described by Garrey³ who observed that when the ventricles fibrillated, the auricles beat in a disordered fashion. We have obtained results similar to Garrey's in a number of experiments, the curves of which are now reproduced. It is not the present purpose to discuss the nature of ventricular fibrillation but to show the relation of the sinus node to this rhythm of the auricles.

The observations were made in the course of the experiments on the function of the sino-auricular node recorded in the preceding communication; the protocols of the experiments given in detail, are also to be found there. The experiments are grouped here according to the sequence in which the three operative procedures, excision of the node, induction of ventricular fibrillation, division of the *A-V* bundle, were undertaken. Table 1 shows this grouping and gives references to the curves in the previous communication.

Group A. When the sino-auricular node was excised, the stoppage phenomenon resulted and was followed by a slower rate of contraction. If fibrillation of the ventricles occurred spontaneously, or was induced by a faradic current, the auricles beat in a disordered fashion. That this disordered rhythm must have been due to ventricular fibrillation is proved by the fact that after division of the auriculo-ventricular bundle, the auricular rhythm became regular after a short interval. Fig. 10 from Experiment 576 shows the stoppage phenomenon. Fig. 14 and 15 from Experiment 584 show the remaining phenomena except for the differences explained in some detail in the protocols.

Group B. If the order of the operative procedures was reversed and fibrillation of the ventricles took place before the excision of the sino-auricular node, then the auricular contractions maintained a regular rhythm and complete irregularity did not occur. If the sino-auricular node was then excised the auricular rhythm became completely irregular. When the auriculo-ventricular bundle was divided as in the preceding group of cases the auricular rate became regular. Curves 20 to 22 from Experiment 589 illustrate these events.

Group C. If the ventricles were fibrillating and the auriculo-ventricular bundle was divided, the auricular rhythm remained regular. When the sino-auricular node was excised, the phenomena usually observed on excising

the sino-auricular node resulted, that is to say stoppage and a slower rate. Fig. 23*a, b* and *c* from Experiment 590 illustrate the foregoing occurrences.

A number of exceptions to these general statements are found in the protocols. A detailed analysis of these exceptions is unnecessary here. These cases are indicated in Table II. The variations in general serve as control experiments.

CONCLUSIONS.

(1) The sino-auricular node maintains the regular rhythm of the auricles, even in the presence of ventricular fibrillation. It is recalled that fibrillation of the auricles is accompanied by complete irregularity of the ventricles. (2) When the sino auricular node is excised and the ventricles are fibrillating, the auricles assume a completely irregular rhythm, just as do the ventricles when the auricles fibrillate. (3) That the assumption of complete irregularity by the auricles is due to ventricular fibrillation, is proved by the fact that when the auriculo-ventricular bundle is divided, the auricles resume a regular rhythm. (4) The auriculo-ventricular bundle conducts impulses, which are the result of fibrillation, in a reverse direction.

TABLE II.

Group	First Event.	Second Event.		Third Event.	Numbers of the Experiments.	Variant Expts*
A 1	Excision of Node	Fibrillation of Ventricles			580-581-582	582
2	Excision of Node	Fibrillation of Ventricles		Division A-V Bundle	575-[576]-583 Fig. 10, 14, 15	
3	Excision of Node	Fibrillation of Ventricles	Incision to A-V groove	Division A-V Bundle	[584] Fig. 14 & 15	
		Incision to A-V groove	Fibrillation of Ventricles		586	
B 1	Fibrillation of Ventricles	Excision of Node			578-579-588	579
2	Fibrillation of Ventricles	Excision of Node		Division A-V Bundle	577-[589] Fig. 20-22	577
C 1	Fibrillation of Ventricles	Division A-V Bundle		Excision of Node	587-[590] Fig. 23	587-590

* Reference to the protocols will explain the nature of the abnormality. The variation in several instances is in the nature of a control.

† The numbers of experiments which are bracketted are those which have been chosen for illustration by curves. It is apparent that groups A-1 and B-1 are represented adequately in groups A-2 and B-2.

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SOME DETAILS OF THE AURICULAR PRESSURE CURVES OF THE DOG.

BY J. G. VAN ZWALUWENBURG AND J. H. AGNEW.

(From the Department of Internal Medicine, University of Michigan.)

EARLY physiological researches^{6 & 13} and more recent clinical work^{9 & 11} have established the general forms and the essential resemblance of the intra-auricular pressure curves, oesophageal cardiograms and jugular tracings. In addition to the waves generally recognised and designated *a*, *c* and *v* by Mackenzie, other undulations lying between the *a* and *v* waves have been described from time to time by various authors, notably Bard,¹ Piersol,¹² Hering,⁷ and Rihl.¹⁵ As yet, however, no general agreement is apparent concerning the location of such waves. The uncertainty regarding the existence and significance of these additional waves has been due in part to the fact that the instruments, commonly used for recording cardiovascular movements, have so much inertia that they may modify the form of the curves or may themselves introduce oscillatory waves into tracings. Furthermore, accurate timing is made difficult by the uncertain delay in the transmission of waves to the neck and by the possibility that pressure changes in the two sides of the heart may not be exactly synchronous.

The exhaustive studies of O. Frank^{4a} led him to substitute an imponderable beam of light for the ordinary writing lever of the Marey tambour. In one form of his instrument (Spiegelmanometer) a small plane mirror is cemented to a delicately constructed lever near the axis of rotation of the latter. The extremity of the lever rests lightly upon the surface of the rubber membrane of the manometer. When this system is displaced by the movement of the membrane, restitution is effected by the force of gravity. In another type of instrument ("Herztonkapsel") a short light hard rubber bar bearing a similar mirror is cemented directly to the membrane, thereby utilizing its elasticity as a restoring force. Because of the reductions in the masses and the radii of rotation of the moving parts, the moments of inertia of these instruments are greatly reduced, their inherent oscillations become very rapid, and they follow cardiovascular movements with great precision. Edens³ and Ohm¹¹ have applied this method to a study of tracings from man, but the complexity of the finer waves makes it desirable to use the method on animals. So far as we know, records of this character have not been published although Frank and Hess⁵ have given a diagram to represent the intracardiac pressure changes obtained by this method.

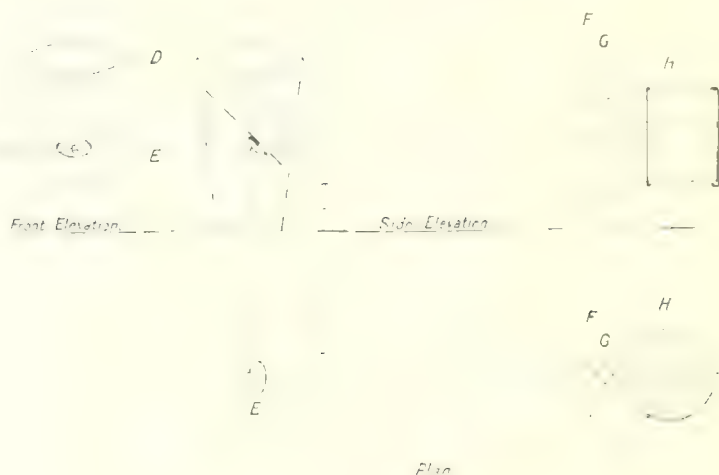
METHODS.

Mirror recorders on the principle of the "Herztonkapsel" were improvised from materials at hand and installed before a small window in a photographic dark room. The essential features of the installation will be appreciated

FIG. 1. DIAGRAM OF APPARATUS.



- A. Filament of Nernst Lamp.
 - B. Cylindrical lens (test tube filled with water).
 - C. Electric time marker, ten vibrations to the second.
 - D. Achromatic lens, two inch diameter and twenty two inch principal focal length.
 - E. Mirror recorders.
 - F. Vertical linear shutter, adjustable.
 - G. Vertical cylindrical lens, $\frac{3}{4}$ inch glass tube filled with water.
 - H. Kymograph.
- (F, G, and H. are installed in a photographic dark room).



from the diagram. Although our mirrors weigh many times the 2 mg. of Frank's instrument,¹ by using a heavier rubber membrane under considerable tension, oscillation frequencies of 120 to 190 per second were readily attained. A graphic method of determining the vibration frequencies of the recorders was devised, depending on the principle of resonance, viz.: the greatest excursion occurs when the frequencies of the recorder and the sound

recorded are equal. The singing voice was recorded and the vibrations per second estimated at the point where the excursion was the greatest. To obtain a basis for the calculations of delays between the several recorders an attempt was made to determine the velocity of transmission in the rubber tubes connecting the receivers and recorders. Two entirely different methods gave values of approximately $\cdot003$ and $\cdot0038$ seconds per metre of 4 mm. rubber tubing. It may be noted that the equivalent rate for sounds in the open air is given as $\cdot00303$ seconds per metre. Although such small intervals are almost negligible, we have none the less kept all our transmission tubes of the same length.

When tested in connection with the recording apparatus, assembled and complete for an experiment, the record of a single impulse was followed by two sets of waves, the one having the frequency of the recorder and the second apparently produced in the recording and transmitting systems and varying from 55 to 80 per second in the different systems.

Four mirror recorders installed in a single cone of light, made it possible to obtain four simultaneous records. An electrically actuated time marker, making a complete oscillation in one-fifth of a second, obscured the whole of the light twice during this interval, every alternate mark therefore indicates a complete oscillation of $\cdot200$ second duration. In the figures, the time marker is shown as an interruption of the line. All the lines in a given curve are interrupted in this manner absolutely simultaneously.

The receiving instruments varied according to the pressures to be examined. Pressure curves from the right auricle were obtained by a modified Chauveau¹⁰ auricular sound introduced through one or other jugular vein into the right auricle. The intra-auricular balloon was inflated to any desired point by means of a water manometer, and the recorder was protected from this pressure by the introduction of a shallow air chamber



Fig. 2. Carotid receiver.

divided transversely into two portions by a rubber membrane. The rubber balloon of the œsophageal sound was stretched over an expansile steel spring adjustable from the oral end. The carotid artery was ligatured and the severed cardiac end was introduced into a glass T-tube which was provided with a rubber cuff at each extremity (Fig. 2). This tube was rigidly clamped to the table in order to prevent gross movements. The cardiac impulses and jugular tracings were received by ordinary funnel receivers and the "heart sounds" by a phonendoscope loosely suspended against the chest wall.

Numerous records were obtained from four dogs, which had been anesthetized with morphine and chlorotone. In most of these the carotid curves and the "heart sounds" were taken and the remaining tambours were used for records of the external cardiac impulse, the jugular waves, the oesophageal cardiogram (left auricle), and the intra-auricular pressure curve (right auricle). Satisfactory simultaneous records of the jugular pulse and right auricular pressure curve at one time, and of the two auricles at another were obtained from the last dog. All records were taken without opening the thoracic cavity.

Recognition of auricular waves.

To recognise auricular waves, they must be compared with known and fixed events in the cardiac cycle. We found our records of heart sounds inadequate for this purpose. Apart from the fact that our records probably represent accompanying shocks as well as the sounds themselves, the onsets of the sounds are not recorded in most instances with sufficient exactitude to be useful for accurate measurements. On the other hand, the beginning of the carotid pulse and its well marked dicrotic incisure furnished definite points of departure for careful measurements. If the exact transmission time of these waves from the heart to the neck were known, these points would give an exact record of the opening and closing of the aortic semilunar valves. The uncertain and probably variable delay, due to transmission from the aortic valves to the neck, introduces an element of uncertainty into fine calculations. The estimated delay to the neck, on the assumption that the arterial wave travels seven meters per second and that this distance is 14 cm., would be 0.020 seconds. Direct measurements were made in one animal by comparing the carotid tracing with an arterial pulse obtained by means of the oesophageal recorder and from this we estimate that the total delay to the carotid must be in the neighbourhood of 0.025 seconds. Finally, in a few instances, where the record of the second sound shows an abrupt onset the time to the dicrotic incisure of the carotid measures from 0.025 to 0.028 seconds.

Our tracings have been very carefully measured by means of hair line, lens, and vernier, in tenths of a millimeter from a selected time mark and have been calculated to thousandths of a second; these values have been written upon the tracings reproduced. All readings were calculated and tabulated before the time intervals were examined. Taking into consideration the vibration times of the recording instruments and the fact that the estimation of an interval involved four readings with time calculations, we believe that the error in the estimated intervals rarely if ever exceeded 0.006 seconds.

General form of auricular tracings.

While the general form of the auricular tracings obtained by this method did not differ materially from that described by others, a number of finer waves were obtained. The auricular wave (*a*) (Fig. 3) is always conspicuous

and is frequently notched, as a result, we believe, of inertia phenomena in the fluid masses in the auricle and great vessels.

The a wave on the œsophageal tracing varies somewhat with the position of the sound receiver. In our opinion the receiver should lie behind the upper portion of the left auricle and all the tracings reproduced are from this position as demonstrated by autopsy. The contraction of the left auricle is usually marked by an early positive followed by a longer negative wave. Its beginning is never sharply marked. Under certain unknown conditions (Fig. 4) a single long gentle elevation appears, which begins considerably before the auricular wave on the right intra-auricular tracing and therefore is not due to auricular contraction. The beginning of the auricular contraction is probably marked by the small notch indicated in the figure and the preceding rise is probably analogous to the stasis wave of the jugular pulse.

The c and v waves are double crested and for convenience we shall speak of the crests as the c_1 and c_2 and the v_1 and v_2 waves, the numerals referring to the first or second crests of the principal waves. Quite commonly also, a series of other waves lies between the c and v waves, for which we are unable to give an adequate explanation. Their duration is too long to be accounted for by instrumental oscillation, and they will not be further discussed. Not infrequently a positive wave appears late in diastole which is probably the equivalent of the h wave of Hirschfelder.⁸

Cause of double crests on the "c" and "v" waves.

At first sight one might assume that the double crests on the c and v waves were due to secondary oscillations arising either in the instruments or the cardiovascular system. We have discarded this supposition on the grounds that (1) the phenomenon is very constant in these positions and occurs nowhere else; (2) the intervening period is greater than that determined for instrumental oscillations and greater than that of other small waves on the tracing; (3) the interval is variable; (4) the second wave may be greater than the first, therefore it does not follow the rule for secondary oscillations, which decline in size; and (5) it is possible to refer them to events in the cardiac cycle.

In attempting to establish a definite time relation between the small crests on the c and v waves on the one hand and the rise and dicrotic incisure of the carotid artery on the other, it is soon found that tracings from the right auricle are unsatisfactory, because the time relations vary considerably and quite unaccountably.

When the carotid tracing is compared with that of the left auricle (œsophageal cardiogram), however, definite time relations can be established. The second crest of the c wave (c_2) (Fig. 4, 5, 6) is found to precede the onset of the carotid pulse by an interval which varies from 0.019 to 0.028 seconds and averages 0.023 seconds (ten measurements), while the first crest of the v wave (v_1) precedes the dicrotic notch by an interval which varies from 0.017 to 0.028 seconds and averages 0.022 seconds (eleven measurements).

These relations are so constant in the same animal and the intervals are so nearly those that correspond to the transmission of the arterial waves from the beginning of the aorta to the carotid that we believe that these two crests, c_2 and v_1 respectively, correspond in time to the opening and closing of the aortic semilunar valves. It is worthy of note that where a definite shoulder precedes the dirotic incisure of the carotid the descending limb of the incisure shows a duration approximately equal to the ascending limb of c_1 .

Of the remaining two crests, that of c_1 precedes the carotid rise by an interval which varies from 0.055 to 0.102 seconds, with an average of 0.072 seconds (ten measurements). Since the semilunars open only .025 seconds before the wave reaches the neck, the crest c_1 must occur from .030 to .077 seconds before this event. It is therefore definitely presphygmic and we have attributed it to mitral closure. The final crest, v_2 , occurs from 0.007 to 0.025 seconds after the dirotic notch on the carotid artery. It is therefore definitely postsphygmic and we have attributed it to mitral opening. The time relations of these waves harmonise with the explanations proposed for the production of the c and v waves: the upstroke of the former corresponding to the beginning of ventricular systole and closure of the auriculo-ventricular valves: the final summit of the latter corresponding to the opening of these valves and the first rush of blood from the auricles to the ventricles. As an explanation for the notched character of the v wave, we would suggest that the down stroke of c_1 is due to the elastic recoil of the mitral valves and the upstroke of c_2 to the momentary increase in pressure which precedes the opening of the aortic valve at the time when the opposing force of the inertia of the blood in the ventricle and great vessels is greatest. The conspicuous fall after the c_1 may be assigned to the causes usually given for the fall during early systole: *i.e.*, auricular diastole, descent of the auriculo-ventricular septum, &c. Likewise the general tendency to a rising pressure in the later part of systole differs in no respect from that seen on tracings taken by other methods. The more abrupt rise that marks the onset of v_1 , corresponding to the sharper carotid fall which precedes the dirotic notch, probably coincides with the cessation of ventricular effort and relief from the distorting effect of the outflow upon the ventricular shape. The shock of semilunar closure, administered by a downward force directed against the point of insertion of the valves, probably carries a portion of the auricular floor with it, thus causing a momentary decrease in intra-auricular pressure. The final fall corresponds to that seen in ordinary tracings. We offer the above explanations in order to show that the notched character of the chief waves can be brought into accord with existing theories as to the events in the cardiac cycle.

Lack of synchronism between the waves of the two auricles.

The difficulties encountered in attempting to refer the waves of the right auricle to the fixed points of the carotid pulse have already been alluded to. The cause of these difficulties becomes apparent when the pressure curves from the right auricle are recorded simultaneously with the œsophageal

cardiograms. From Fig. 3, 4 and 5, it will be seen that the fine waves in the two auricles are rarely synchronous, and that the discrepancies frequently exceed what we regard as allowable limits of error. Indeed it is at times difficult to identify homologous waves of the two auricles. This was constantly true of the v waves in the last dog examined and throughout our tracings from this animal the main fall in pressure in the right auricle at the end of systole begins before the dicrotic incisure of the carotid, whereas the v_2 of the left auricle always occurs after the incisure. If we assume that the former represents the v_2 of the right auricle, then periods of 0.03 to 0.06 seconds must have intervened between homologous events in the two sides of the heart, at the end of ventricular systole; a condition analogous to that which gives rise clinically to a reduplication of the second heart sounds. Einthoven² states that the records of distinct reduplication of the second sounds often show 0.01 to 0.03 seconds of complete rest between the two components; and Weiss and Joachim¹⁶ speak of an interval of 0.06 second. Since these figures refer to the periods of silence, and not to differences in the times of onset of the sounds, the lack of synchronism is quite as marked as in our last dog. In our opinion slight discrepancies in time between homologous waves on the two sides of the heart are very common.

In Fig. 6 there are three waves at the beginning of each systole, the first being larger on the œsophageal tracing, the second larger on the right auricular and the third conspicuous on both. In such a case it seems probable that the mitral valve closed before the tricuspid and that each produced a large wave in its own auricle and a smaller wave on the opposite side.

Comparison of jugular and right auricular tracings.

Tracings from the right external jugular vein of the dog (Fig. 6 and 7) in most instances showed the three usual waves; the a and v waves being particularly well marked. Comparison with simultaneous tracings from the right auricle, obtained by introducing a sound through the left jugular, shows that the delay in transmission is considerable and variable. For example, in three curves selected at random from the same experiment, the delay of the a waves is 0.079, 0.096 and 0.112 seconds, respectively; while the delay in the v waves is 0.173, 0.247 and 0.278 seconds. Furthermore, in the dog the finer waves of the auricular tracing are usually lost in the jugular vein. This is probably due to the interposition of a valve at the junction of the external jugular with the brachio-cephalic vein. When the force and duration of the waves from below is sufficient to overcome the combined forces of the venous pressure and the inertia of the moving column of blood, the valves are closed. The volume of blood will then increase at a fairly uniform rate in the vein and the ascending limb of the resulting tracing will move upward in a line whose inclination to the horizontal gradually diminishes as the vein fills and the pressure within rises. These conditions are seen to be almost fulfilled in our jugular tracings from the dog (Fig. 8). The upstrokes of the principal waves are practically parallel, the lower portions being slightly more vertical than the upper portions. The

tracings from the external jugular vein of the dog therefore show the characteristics of stasis waves.

In man it is usually possible to obtain a venous tracing over the jugular bulb, below the point at which valves break the continuity of the blood column, and one may therefore expect that the finer details of the intra-auricular curves will be recorded on the jugular pulse under favourable circumstances. The exact interpretation of these finer waves is difficult on account of the uncertain delay of their transmission to the neck, the interference of carotid or other arterial pulsation and the lack of synchronism between the events in two sides of the heart.

CONCLUSIONS.

1. By means of the mirror recorder of O. Frank, waves may be demonstrated on the œsophageal cardiogram of dogs which bear a definite relation to the opening and closing of the aortic semilunar valves. These waves cause a bifurcation of the ordinary *c* and *v* waves.

2. Pressure curves from within the right auricle show waves in every way similar to those in the œsophageal tracing and are referred to analogous events on the right side of the heart.

3. The waves in the two auricles are not exactly synchronous, and the phenomena on the right side of the heart cannot be accurately correlated with those on the left.

4. The pulsations in the external jugular veins of the dog show the characteristics of stasis phenomena.

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Fig. 3. Schematic diagram of the experimental setup.

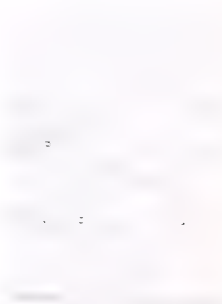
Fig. 4. Schematic diagram of the experimental setup. The diagram shows the arrangement of the components used in the experiment, including the source, the sample, and the detector.

Fig. 5. Schematic diagram of the experimental setup.

Fig. 6. Schematic diagram of the experimental setup.

Fig. 7. Schematic diagram of the experimental setup.

Fig. 8. Schematic diagram of the experimental setup.



OBSERVATIONS UPON THE EFFECTS OF STROPHANTHIN IN CASES OF AURICULAR FIBRILLATION.*

By C. D. S. AGASSIZ.

(From the City of London Hospital for Diseases of the Chest.)

THE first account of the intravenous administration of strophanthin as an alternative to digitalis in cases of heart disease is by Fraenkel.² He noted increased amplitude and slowing of the pulse, and diuresis as a result of the injection of strophanthin. The dosage employed by him was usually 1·64 grain (1 milligramme) which he stated should not be repeated for 24 hours. Other writers (Liebermeister,⁶ Hoepffner,¹ Flesch,³ &c.) have used strophanthin, chiefly in cases of heart disease, in doses of from 1·256 grain (.25 milligramme) to 1·33 grain (1·9 milligrammes) and their results were similar to those obtained by Fraenkel. Few of these writers, however, give graphic records of the cases treated with strophanthin and, apart from these and from the statements of the beneficial effects which follow and the dosage employed, no sufficiently clear indication is given as to the type of case which reacts most conspicuously. Flesch³ gives radial and venous curves from a case treated with strophanthin and these curves are evidently taken from a case of auricular fibrillation. Bailey¹ reports a case of auricular fibrillation treated with strophanthin and Zwahlenburg⁵ records the results obtained by the use of strophanthin upon three cases of auricular fibrillation.

For a number of years digitalis has been known to produce striking results in cases of cardiac failure, but the type of case in which it acts so beneficially has only been isolated within recent years by the work of Mackenzie.⁷ The success which has attended digitalis administration is very largely attributable to its action upon a definite group of clinical cases, which are now classified as instances of auricular fibrillation,⁵ and a considerable advance in the therapy of heart affections has been made by the isolation of this group and the discovery of the specific action of digitalis on it. It is well known that a large proportion of patients who have auricular fibrillation show a conspicuous and beneficial reaction to the drug, while patients who do not suffer from this cardiac disorder are either affected to a far less extent or actually harmed by its employment.

Observations.

The present investigation has been pursued along lines indicated by Mackenzie's work. The object has been an inquiry into the action of strophanthin on that group of cases, namely, auricular fibrillation, in which the allied drug, digitalis, is so effective.

* The observations were made at the suggestion of Dr. T. Lewis to whom I am much indebted for assistance. I am also indebted to Dr. W. J. Hadley for permission to publish the clinical notes of the cases and to Dr. W. W. Jameson for many valuable suggestions.

Cases presenting the complete irregularity which accompanies auricular fibrillation were alone investigated and in each case the nature of the irregularity was established by polygraphic tracings taken on numerous occasions. In all seven cases have been investigated. It has not been

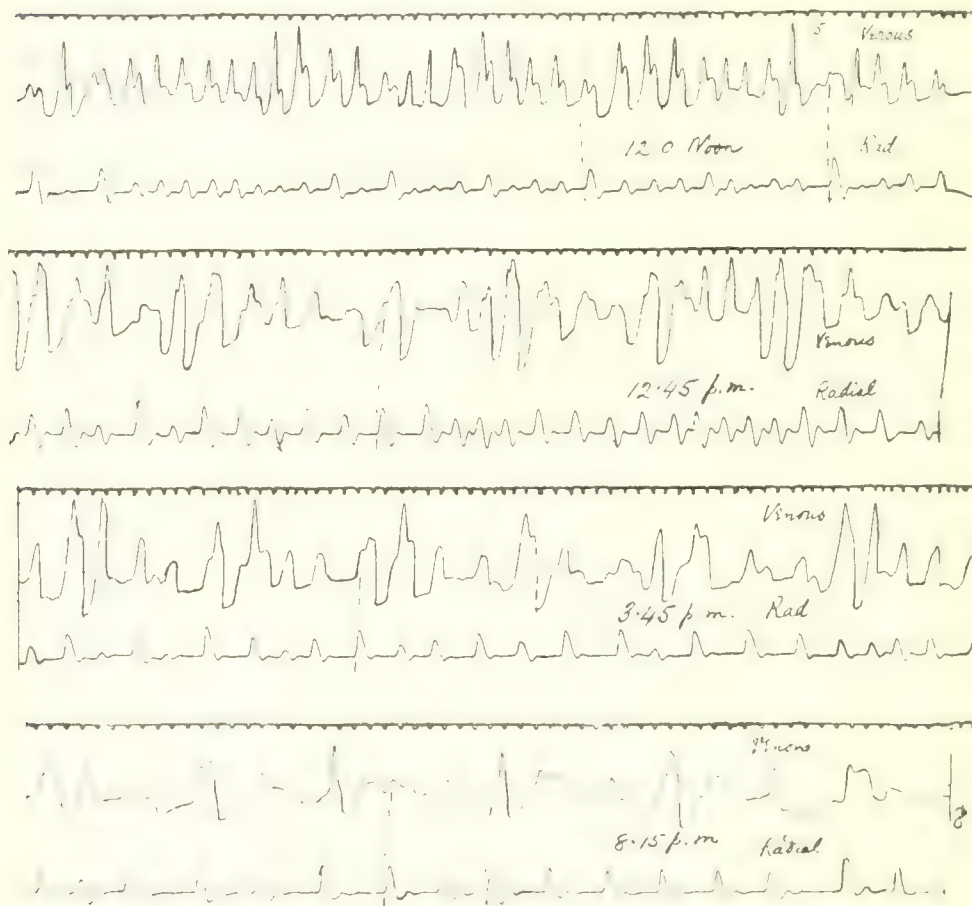


Fig. 1. Four polygraph curves from CASE 5, taken on October the 7th, 1911. Injections of strophanthidin 1.250 gram were given at 12.22 p.m. and 3.22 p.m. and a third of .500 gram at 6.25 p.m. The curves correspond to the hours 12.0 noon, 12.45, 3.45 and 8.15 p.m., respectively. The rates for the full half minute at these times were 160, 132, 110 and 82. In each tracing gross irregularity of the pulse, and the ventricular form of venous pulse is shown.

considered necessary to give curves from each case. A few curves (Fig. 1) from one case (CASE 5) are given as examples: the curves from the other cases were equally characteristic. Throughout these investigations I have taken a gross irregularity of the heart beat accompanied by the ventricular form of venous pulse as a criterion that auricular fibrillation⁵ was present. The stated heart rates have been calculated, without exception, from curves taken from the patients. Where the venous or apex beat rate did not

correspond to that of the radial pulse, one or other of the first two has been used as an index of the true rate of heart beat. In the great majority of cases the heart rates per minute have been calculated from strips of curve of not less than 30 seconds duration.

Before administering strophanthin to any patient an interval of at least four days elapsed, from the date of admission. During this time the patient remained in bed and no drugs of the digitalis group were given. Sufficient time was allowed for the excretion of any drug given previous to admission. The strophanthin employed was that sold by Messrs. Burroughs, Wellcome & Co. It is sent out in tabloid form, each tabloid containing 1/500 grain of strophanthin.

Method of administration. The syringe, needle, measures and test tubes having been sterilised by boiling for 15 minutes, the required dose of strophanthin was dissolved in normal saline solution (1 in 8,000) and this was then drawn up into the syringe, care having been taken to expel all air bubbles from the syringe before injection. A bandage was applied tightly to the upper arm and the front of the elbow was cleansed in the usual way. A prominent vein was selected and the needle was pushed gently into it. The bandage was then loosened and the solution slowly injected. The time taken to inject the whole of the solution has been from a half to one minute.

Results of injections. In all, the results of 45 injections have been observed. The dosage employed varied from 1 500 grain to 1 250 grain. In some instances isolated injections were given, in other cases the injections were repeated at intervals of 1 to 3 or more hours. In the majority of cases it is unnecessary to inject more than 1/250 grain in order to obtain slowing of the pulse, often of considerable extent, slowing which can be maintained and increased by repetition of the injection.

In my earlier observations I adopted what was considered a perfectly safe dose, namely, 1 500 grain, and injected it into three patients (CASES 2, 3 and 4) watching the subsequent effect on the heart rate. The effect of such a dose is insignificant, the heart rate falling as a rule by not more than 10 to 20 beats per minute and this effect being transient.

The following are examples of the results obtained :—

	INITIAL VENTRICULAR RATE.	FULL EFFECT.	REMARKS.
CASE 2	142 per minute.	136 per minute.	Subsequent injections given on same day.
CASE 2	136 ..	134 ..	
CASE 3	130 ..	104 ..	
CASE 4	124 ..	108 ..	After 16½ hours.
CASE 4	118 ..	103 ..	
CASE 4	104 ..	96 ..	
CASE 4	100 ..	114 ..	Subsequent injections given on same day.
CASE 4	103 ..	94 ..	

It became apparent that single doses of 1/500 grain are insufficient therapeutically and consequently this dose was repeated at intervals of one hour, four or five injections being given. Providing that the heart rate is rapid

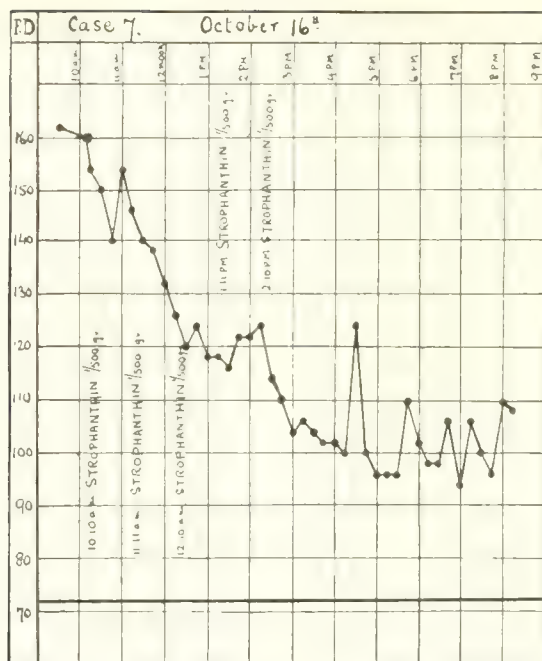


Fig. 2. CASE 7. Illustrating the rapid fall of rate which occurs when injections of 1/500 grain are given at intervals of one hour; the full details of this patient, and of others charted, will be found at the end of this paper.

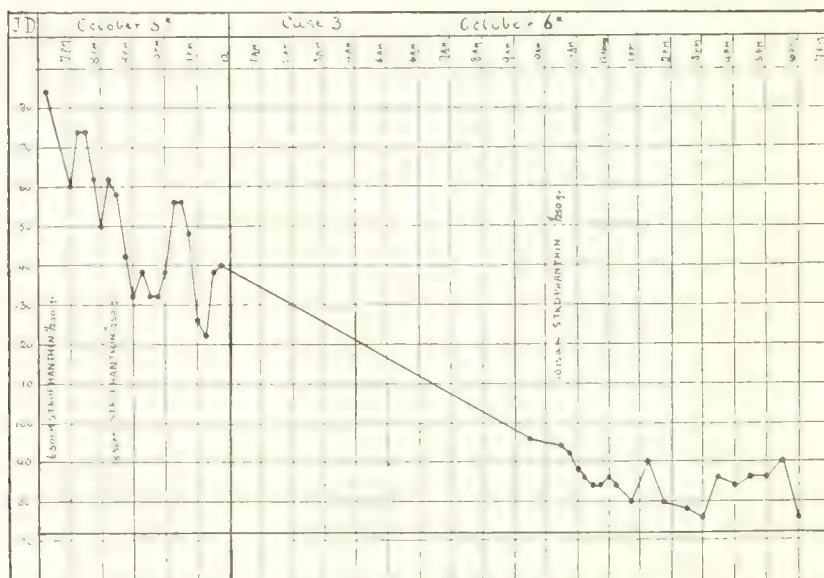


Fig. 3. CASE 3. Illustrating the fall of ventricular rate after two injections of 1/250 grain, separated by an interval of 2 hours. The heart rate fell from 184 to 96 per minute within 15 hours.

a series of such injections produces a considerable fall of ventricular rate, which occurs in steps, following the separate injections; so that even in the instance of a rapid heart the rate may be reduced almost to the normal shortly after the last injection is administered. (Fig. 2.)

When the initial ventricular rate is slower, this method of administration seems to produce but slight retardation.

	INITIAL VENTRICULAR RATE.	FULL EFFECT OF REPEATED DOSES.	REMARKS.
CASE 3	122 per minute.	100 per minute.	Not attained until 6½ hours after last injection. Four injections given.
CASE 7	124 per minute.	112 per minute.	Two injections of 1/500 grain each given. Rate not further reduced until 1/250 grain given.

The injection of doses of 1/500 grain in series has the disadvantage that the dose needs frequent repetition at relatively short intervals. Consequently a larger dose was employed, 1/250 grain being administered, at first as a single injection. The actual result is variable, but a striking fall of ventricular rate almost always occurs (Fig. 5) and usually amounts to 20 to 40 beats per minute. The fall commences promptly after the injection and is steepest during the first half-hour, but it may be continued for 24 hours.

	INITIAL VENTRICULAR RATE.	FULL EFFECT.	TIME REQUIRED FOR FULL EFFECT.
CASE 3	114 per minute.	84 per minute.	5½ hours
CASE 5	178 ..	134 ..	24 ..

But it is only rarely that 1/250 grain yields the desired effect, namely, re-establishment of the normal heart rate. A second injection of 1/250 grain, given within two or three hours of the first, produces further slowing and normal heart rates are almost reached. The fall after the second injection is generally greater than that which succeeds the first, but it must be remembered that when the second injection is given the ventricular rate is still falling as a result of the first injection. Even two doses of 1/250 grain each are often insufficient to abolish the tachycardia, though the pulse may often fall to 90 or 100 per minute. It may be necessary to give a third dose of 1/250 grain or 1/500 grain to complete the effect. The accompanying charts (Fig. 3 & 4) illustrate the conspicuous falls of pulse rate which occur when strophanthin is administered in this manner.

Thus the desired result may be obtained as a rule by two or three injections of 1/250 grain given over a period of 4 to 9 hours. Necessarily the required dosage is not constant from case to case; in one case a single dose, in others two doses of 1/250 grain, are sufficient, while in yet others an extra 1/250 grain or 1/500 grain must be given before the heart rate is reduced to normal (Fig 3 & 4). More than three injections are as a rule unnecessary.

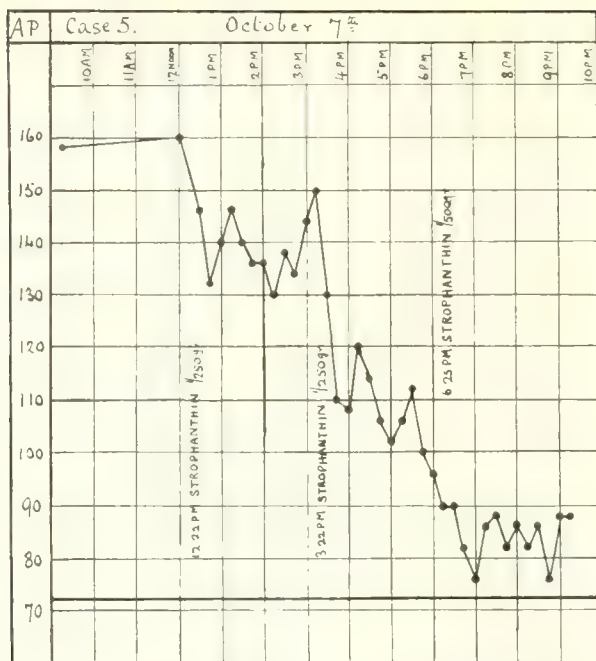


Fig. 4. CASE 5. Showing the rapid fall of ventricular rate produced by two injections of 1/250 grain and one of 1/500 grain given at intervals of three hours. The abrupt fall during the thirty minutes following each injection is very clearly shown. This chart illustrates the return to normal from a rapid rate shortly after the last injection of strophanthin.

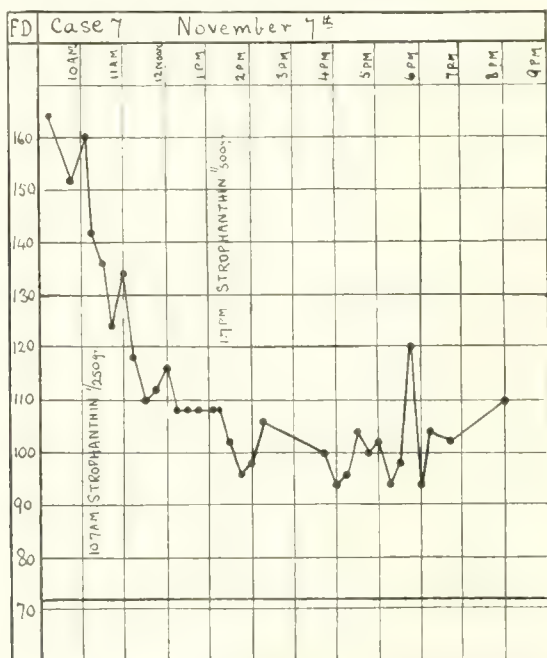


Fig. 5. CASE 7. Illustrating the effect of an injection of 1/250 grain, followed after three hours by one of 1/500 grain. The effect of the first injection on the heart-rate was very considerable.

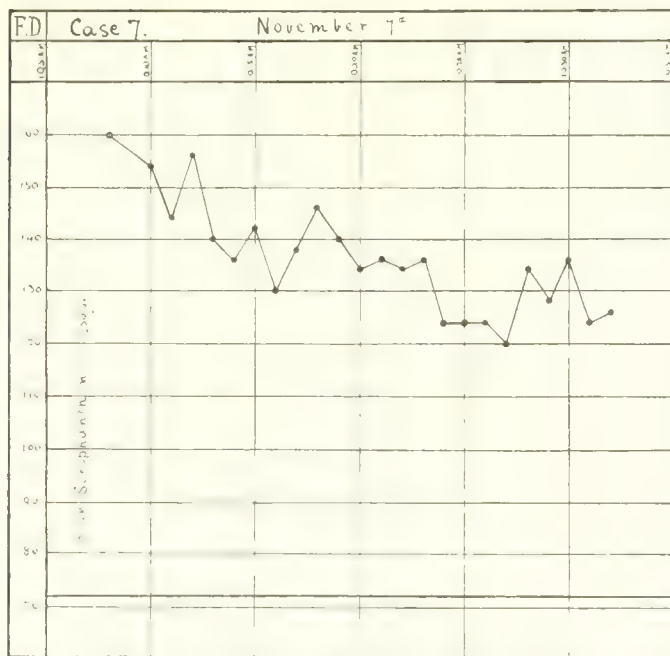


Fig. 6. CASE 7. Compiled from a tracing taken continuously for 24 minutes after an injection of 1/250 grain (the first injection shown in Fig. 5). It shows clearly the immediate and uniform effect of strophanthin on the heart.

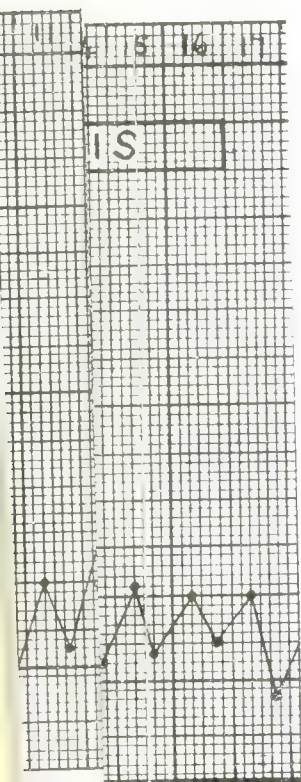
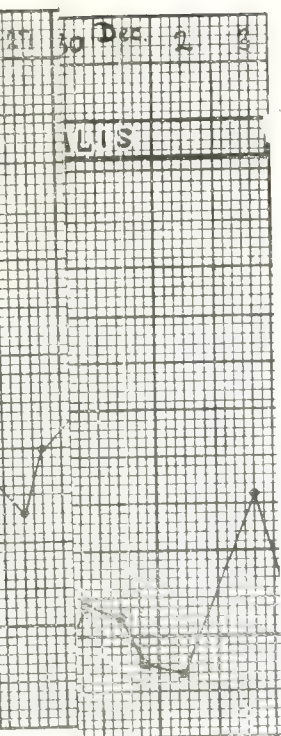
The permanency of effects. After a single injection of 1/250 grain the slowing of the heart rate persists for 12 to 60 hours (CASES 3 and 5), after which time there is a gradual return towards the original rate. If the ventricular rate is reduced to the normal, by two or more doses, the slow action of the heart is maintained for a variable period of from 3 to 10 days. The duration of the effect seems to depend upon the degree of slowing of the heart rate rather than upon the method of dosage adopted or the total amount of strophanthin given. The acceleration which follows is spread over a week or a longer period and eventually the rate re-attains the level at which it stood originally. If extra doses are given during the period of acceleration, the reaction is prompt and conspicuous; the heart slows once more. A characteristic illustration of this gradual acceleration of heart beat and the abrupt drop after the administration of strophanthin is shown in the accompanying charts (Fig. 7, CASE 7; Fig. 8, CASE 3).

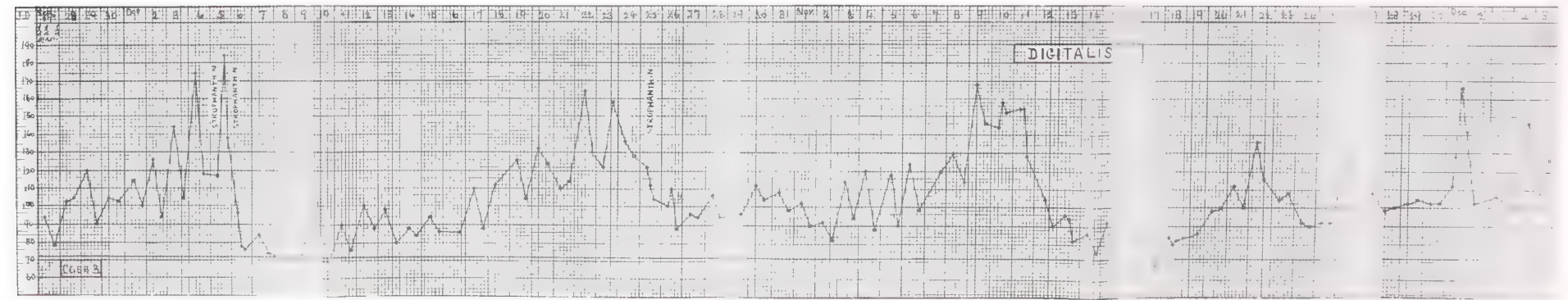
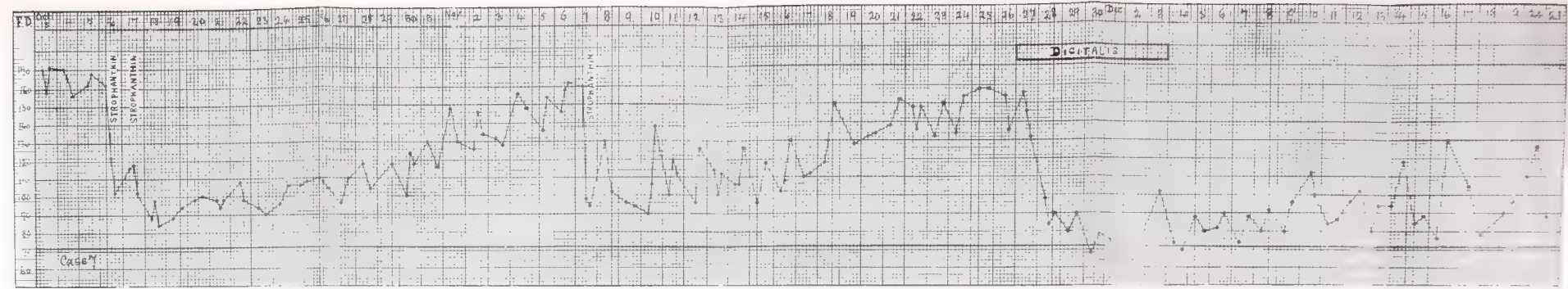
It is unnecessary to reduce the rate of heart beat lower than 90 to 100 per minute, for, as soon as this has been accomplished, the symptoms of distress rapidly disappear and as the effect lasts for from 3 to 10 days, or longer, more than a sufficient armistice is established during which, in a case of urgency, the heart may be brought under the full influence of other members of the same group of drugs.

Other effects produced by strophanthin injection. The general condition of the patient shows an almost immediate improvement. Cyanosis, when present, diminishes or completely disappears and the sallow or ichteroid complexion gives place to one of more healthy colour. When dyspnoea is originally present it quickly disappears and within a few hours an orthopnoeic patient may lie flat in bed without discomfort, and with an almost normal respiratory rate. In those patients who are wakeful, the reaction of the heart is accompanied or followed by sleep within a few hours. Oedema, when present, quickly vanishes. An enlarged liver decreases rapidly in size. Coupling of the ventricular beats occurs but rarely (it was seen for a brief period in CASE 1). An appreciable decrease in the extent of the deep cardiac dullness was only observed in one case (CASE 6). In cases in which a full diastolic bruit is present on admission this bruit becomes early diastolic in time when the heart rate returns to normal. In some cases strophanthin produces a conspicuous diuretic effect. Mackenzie noted in his paper that digitalis only produces an increased flow of urine in cases in which oedema is present. The same statement appears to apply to strophanthin (see CASE 7). In CASE 5 sudden death occurred 12 hours after the last injection of strophanthin; a total of 1·100 grain had been given within the space of six hours. The pulse had been constant at 80 to 90 per minute during the last two hours of observation and nothing abnormal was noted during the night. The patient had slept well and in the early morning she stated that she felt much better. Shortly after this she complained of a pain in her abdomen and a few minutes later dropped back dead. Whether death was due to the strophanthin or not it is impossible to say. Rises of temperature (of 1 to 3 or 4 degrees) on the day of injection or upon the following day occur frequently (CASES 2, 4 and 7) and usually, when injections are given on two consecutive days, the rise of temperature is more evident on the second day. This temperature reaction occurred most readily in a patient who exhibited signs of arterio- and cardio-sclerosis (CASE 4). Pain and transient inflammation at the site of injection, appearing shortly after injection, and persisting for one to two hours, is of frequent occurrence; but it is insufficient to account for the rise of temperature. In two of my cases (CASES 2 and 4) cramp and a feeling of numbness in one or other foot and leg were complained of, but in neither was there any alteration in the appearance of the limb or impairment of sensation; these sensations did not persist for any length of time.

The types which react to strophanthin.

The effect of strophanthin on cases of auricular fibrillation with a rapid heart rate is very similar to that of digitalis, but its action is more rapid. The ventricular rate is profoundly affected in young subjects with a previous history of rheumatism, but cases which give no history of rheumatism also react. In a single instance of arterial and myocardial disease occurring in an elderly subject, the effect on the heart rate was slight and transient and conspicuous rises of temperature occurred after each series of injections.





In one case the auricular fibrillation was paroxysmal (*CASE 6*). Strophanthin reduced the heart rate (Fig. 9), but apparently prolonged the paroxysm.

CONCLUSIONS.

1. Strophanthin, administered intravenously, has a very similar action to that of other members of the digitalis series, when employed upon cases of auricular fibrillation. It is a powerful and serviceable remedy when a rapid reduction of heart rate is desired in cases of auricular fibrillation in young subjects or in those cases which give a history of rheumatism. The heart rate may be reduced from 180 or 160 to 100 or 80 per minute within six or eight hours; the effect is lasting from at least three to ten days (*CASES 3 and 7*).

2. The method of administration, which has been found most suitable, consists of the injection of 1.250 grain, repeated after three hours, and followed after a further interval of three hours by an injection of 1.500 grain, if required.

3. In addition to its effect upon the heart, strophanthin produces diuresis in cedematous patients, and alleviates all urgent symptoms within a very short space of time.

4. The injections may be followed by pain at the site of injection and by a rise of temperature. In one instance a patient died unexpectedly some 12 hours after the injections had ceased.

DETAILED REPORT OF CASES.

CASE 1. C. C., a woman, aged 44. *Auricular fibrillation. Mitral stenosis and incompetence. Great improvement in the general condition and considerable reduction of the heart rate as a result of the administration of strophanthin.*

Admitted on June the 1st, 1911, complaining of shortness of breath, pains in the chest, cough and palpitation.

Family history. Her father died of phthisis and her mother of bronchitis. Two brothers and three sisters are alive and well.

Previous illnesses. She had diphtheria when a child. At intervals during the last 14 years she has had severe attacks of influenza. For the last 8 years she has suffered from rheumatism and bronchitis during the winter months.

History of present illness. Ten weeks ago she began to suffer from shortness of breath and cough, worse at night, with absence of expectoration.

Condition on admission. The patient sits propped up in bed. Both cheeks are flushed and her expression is anxious. Respiration is rapid (30-40 per minute). The apex beat is in the fifth left interspace in the nipple line. The deep cardiac dullness extends from mid-sternum to 1 inch outside the left nipple line. The heart is very rapid in rate (180 per minute) and very irregular in action. Rough diastolic and an indistinct soft systolic bruits are present at the apex. The radial arteries at the wrist are thickened. There is oedema of the bases of both lungs. There is slight clubbing of the finger tips. The liver is not enlarged. There is no swelling of the feet. The urine contains scanty pus cells and granular casts but no albumen. Gross irregularity of the heart's action and the ventricular form of venous pulse are present, as shown by polygraphic records.

Treatment and progress. The patient remained at rest in bed for four days; her condition remained unaltered. On June the 9th, 1/250 grain of strophanthin was given at 11 a.m. and this dose was repeated at 2.20 p.m. Two injections of 1/250 grain each were given on June the 10th at 10.40 a.m. and at 5.40 p.m.; a final dose of 1/250 grain was given at 12.15 p.m. on June

the 11th. During a period of 81 hours the ventricular rate fell from 168 to 48 per minute, a fall of 120 beats per minute. An improvement in her condition became evident after the second injection on June the 9th, and this change became more and more conspicuous as the rate of heart-beat fell. Her appetite returned, her colour improved, respiration became less frequent, the flow of urine increased and she slept almost continuously for more than 24 hours after the second injection on June the 9th. The ventricular rate remained between 50 and 60 per minute for three days but then assumed a rate of 70 to 90 and continued so until June the 23rd, after which it began to increase. On June the 13th, the patient received 30 minims of tincture of digitalis, with 15 minims of tincture of strophanthus. On June the 15th, a slight tendency to grouping of beats was observed and a long rumbling diastolic bruit was present at the apex. All signs of œdema of the lungs had disappeared. On June the 24th, tincture of digitalis in 5 minim doses given three times daily was prescribed but was discontinued on June the 28th, 55 minims having been taken without producing any slowing of the heart-rate. On July the 2nd (heart-rate 135 per minute) tincture of digitalis in 10 minim doses given three times daily was ordered, but was discontinued on July the 4th, a total of $1\frac{1}{2}$ drachms having been taken. On July the 6th, $\frac{1}{50}$ grain of atropine sulphate was injected subcutaneously and the effect on the heart-rate is shown in Table II. There was slight œdema of the base of the right lung on July the 7th. At no time was there any alteration in the extent of cardiac dulness. Fibrillation of the auricle persisted throughout the whole period of observation. The patient was discharged on July the 13th much improved.

TABLE I. (CASE I.)

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG	* URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS
June 5th	3.30 p.m.	180		37	1-inch outside left nipple line	Dyspnoea, palpitation, anoræxia. No swelling of feet. Sleeplessness. Oedema of bases of both lungs.
6th	3.30 p.m.	156		22		
7th	2.50 p.m.	166		42		
8th	11.25 a.m.	158		44		
9th	9.45 a.m.	168		44		
	11 a.m.		Strophanthin 1/250 grain			
	11.40 a.m.	159				
	2.5 p.m.	158				
	2.20 p.m.		Strophanthin 1/250 grain			
	3.5 p.m.	141				
	5.55 p.m.	114				
	11.15 p.m.	99				
10th	10.20 a.m.	118		34		Sleeping. Slept all night. Feeling very much better.
	10.40 a.m.		Strophanthin 1/250 grain			
	11.15 a.m.	114				
	2.25 p.m.	93				
	5.20 p.m.	114				
	5.40 p.m.		Strophanthin 1/250 grain			
	6.35 p.m.	141				
	9.30 p.m.	105				Slept a great deal during the day.
11th	11 a.m.	103		57		Slept all night.
	12.15 p.m.		Strophanthin 1/250 grain			
	12.55 p.m.	91				
	3.50 p.m.	84				
	7.10 p.m.	78				
	10.15 p.m.	91				
12th	9.35 a.m.	70		50		Feels very well.
	1.30 p.m.	58				
	8 p.m.	48				
	11.10 p.m.	48				

* Total amount excreted during 24 hours.

DATE	HOURLY WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES)	REMARKS.
June 13th	9.35 a.m.	55	Tinct. of Digit. m. XXX*	45		
	2.15 p.m.	51	Tinct. of Stroph. m. XV			
	8 p.m.	57				
	11.15 p.m.	48				
14th	9.35 a.m.	53				
	1.40 p.m.	60		48		
	9.45 p.m.	61				
15th	9.40 a.m.	75		52	$\frac{1}{2}$ inch out- side left nipple line.	Lungs clear, tendency to grouping of beats.
	9.20 p.m.	70				
16th	9.30 a.m.	70		38		Feeling very well.
	9.35 p.m.	78				
17th	9.35 a.m.	89		48		
	9.40 p.m.	70				
18th	10.45 a.m.	84		46		
	9.30 p.m.	72				
19th	9.35 a.m.	79		54		
	10 p.m.	77				
20th	9.30 a.m.	85		30		
	9.25 p.m.	85				
21st	9.30 a.m.	85				
22nd	10.30 p.m.	81		58		
23rd	10.15 p.m.	73		30		
24th	10.10 a.m.	96	Tinct. of Digit. m. XV	40		
	9.30 p.m.	83				
25th	11.50 a.m.	92	Digit. accidentally omitted	54		
	9.50 p.m.	70				
26th	9.45 a.m.	114	Tinct. of Digit. m. XV	42		
	9.50 p.m.	91				
27th	10.5 a.m.	103	Tinct. of Digit. m. XV	47		
	9.45 p.m.	93				
28th	9.35 a.m.	103	Tinct. of Digit. m. X (Total taken=m. LV)	51		
	9.35 p.m.	100				
29th	9.35 a.m.	102		42	$\frac{1}{2}$ inch out- side left nipple line.	
	9.30 p.m.	84				
30th	9.25 a.m.	101		54		
July 1st	9.30 a.m.	111		40		
	9.45 p.m.	95				
2nd	9.20 a.m.	135	Tinct. of Digit. $\frac{1}{2}$ dr.	47		Depressed. Weeping.
	9.50 p.m.	88				
3rd	9.40 a.m.	104	Tinct. of Digit. $\frac{1}{2}$ dr.	50		
	8.40 p.m.	90				
4th	9.30 a.m.	80	Tinct. of Digit. $\frac{1}{2}$ dr. (Total, $1\frac{1}{2}$ dr.)	55		
	9.45 p.m.	93				
5th	9.35 a.m.	75		58		
	9.10 p.m.	79				

* The total dosage for the day.

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
July 6th	9.30 a.m.	80	1 50 gr. atrop. sulphate	41		
	9.15 p.m.	99				
7th	9.30 a.m.	87		58		
	9. p.m.	102				
8th	9.30 a.m.	104		52		
	9.30 p.m.	116				
9th	10 a.m.	90		44		Up 2 hours.
	12.35 p.m.	90*				
	10 p.m.	79				
10th	9.40 a.m.	83		37		Up 2 hours.
	9.50 p.m.	80				
11th	9.30 a.m.	85		51		Up 2 hours.
	9.35 p.m.	116				
12th	9.30 a.m.	83		47		Up 2 hours.
	9.30 p.m.	77				
13th	9.30 a.m.	93		47	1 inch out-side left nipple line.	Up 2 hours.
	9.35 p.m.	94	Tinct. of Digit. m. XX.			
15th.						Discharged.

* Rate 15 minutes after returning to bed. Feels well.

TABLE II. (CASE I.)

Results of injection of 1/50 grain of Atropine Sulphate.

DATE.	HOUR AT WHICH TRACING TAKEN.	HEART-RATE PER MINUTE.	REMARKS.
July 6th	1.37 p.m.	96	
	1.58 p.m.	Atropine Sulphate, 1/50 gr.	
	2.0 p.m.		
	2.4 p.m.	93	
	2.6 p.m.	90	
	2.8 p.m.	98	
	2.10 p.m.	107	
	2.11 p.m.	127	
	2.12 p.m.	131	
	2.14 p.m.	140	
	2.15 p.m.	142	
	2.20 p.m.	156	
	2.23 p.m.	149	
	2.24 p.m.	141	
	2.26 p.m.	142	Mouth dry.
	2.29 p.m.	146	
	2.35 p.m.	150	
	2.40 p.m.	145	
	2.45 p.m.	145	Pupils slightly dilated, cheeks flushed.
	2.50 p.m.	150	
	2.55 p.m.	158	
	3.0 p.m.	153	
	3.5 p.m.	156	
	3.10 p.m.	148	
	3.15 p.m.	148	
	3.20 p.m.	138	
	3.25 p.m.	158	
	3.30 p.m.	155	
	3.35 p.m.	162	
	3.40 p.m.	138	
	3.45 p.m.	142	Mouth not so dry.
	3.50 p.m.	138	
	3.55 p.m.	132	

CASE 2, E. L., a man, aged 58. Auricular fibrillation (non-rheumatic) and left pleural effusion. Conspicuous slowing of the heart rate and improvement in general condition following the administration of strophanthin.

Admitted on September the 4th, 1911, complaining of pain in the epigastrium, shortness of breath and severe palpitation.

Family history. No history of any cardiac or lung affection in the family.

Previous illnesses. No previous illnesses. No history of rheumatism.

History of present illness. In December, 1910, he began to suffer from shortness of breath and swelling of the feet. These symptoms became gradually worse until any exertion caused severe palpitation, and, at times, giddiness. Fluid had been aspirated from the left pleural cavity on several occasions during the seventeen weeks preceding admission.

Condition on admission. The patient sits propped up in bed. There is considerable dyspnoea, which becomes extreme if he attempts to lie down. His complexion is sallow, but his cheeks, lips and ears are deeply cyanosed. He is very restless and sleepless and his appetite is bad. The apex beat is diffuse and there is considerable pulsation in the epigastrium. On the left side of the chest there is an area of absolute dullness extending from the right sternal margin round the left axilla to the vertebral column. It is limited superiorly by the lower border of the third left rib in front, by the inferior angle of the left scapula behind, and inferiorly by the costal margin. Skodiac resonance is present just above the limit of dullness posteriorly. Over the dull area there is absence of vocal fremitus, vocal resonance and breath sounds. The heart is very rapid in rate (140 per minute) and grossly irregular in action. At the apex a rough to and fro rub, synchronous with each heart beat, is heard, but no bruit is present either here or at any of the other valvular orifices. The pulse is very irregular in time and force and scarcely palpable. The liver is palpable four fingerbreadths below the right costal margin. There is no ascites or oedema of the feet. The urine contains a trace of albumen. There are present gross irregularity of the heart's action and the ventricular form of venous pulse as shown by polygraphic tracings.

Treatment and progress. There was no improvement in the patient's condition until September the 6th (two days) when three pints of fluid were syphoned off from the left pleural cavity and the dyspnoea decreased somewhat as a consequence, though his condition otherwise remained unchanged. On September the 8th the cyanosis was less evident. There was considerable pulsation of the vessels at the root of the neck. The deep cardiac dullness extended $\frac{1}{2}$ inch to the right and $5\frac{3}{4}$ inches to the left of mid-sternum. There was dullness, absence of breath sounds and vocal resonance over the base of the left lung and a loud pleural rub was heard in the third left interspace in front. The urine was scanty. On September the 9th, the 10th and the 11th, injections of strophanthin were given (Table III) with a result that the ventricular rate fell from 142 to 90 during a period of 45 hours. The condition of the patient immediately improved, the cyanosis became less, the dyspnoea decreased, the appetite returned and he slept almost continuously for 24 hours from the morning of September the 10th. Tincture of digitalis in 15 minim doses given three times daily was prescribed on September the 13th, but was discontinued on September the 22nd, when the ventricular rate had fallen to 62 per minute and a total of $6\frac{1}{2}$ drachms of digitalis had been taken.

The heart rate remained at the same level until September the 28th when an acceleration in rate again became evident. There was an increased flow of urine between the 15th and 25th of September. At the examination on September the 15th, the cyanosis was considerably reduced and the pulsation at the root of the neck had become very much less. The liver extended to three fingerbreadths below the right costal margin and there was some oedema of the base of the right lung. The patient slept well at night, ate his meals heartily, and felt quite well. On September the 22nd the liver was palpable just below the costal margin. The heart was still irregular in action and no bruit was present at the apex. The condition of the base of the left lung remained unchanged. At no time was there any alteration in the extent of the cardiac dullness (other than could be attributed to percussion error). The condition of auricular fibrillation, as shown by polygraphic tracings, persisted throughout the whole period of observation.

TABLE III. (CASE 2.)

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES)	REMARKS.
Sept.						
4th	6.30 p.m.	131				
6th	12.15 p.m.	140				
8th		135		20	$\frac{1}{2}$ -5 $\frac{3}{4}$	Three pints of fluid removed from left pleural cavity. Breathing easier. Slept badly last night.

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG	URINE (IN OZS.)	SIZE (IN INCHES)	REMARKS.
Sept. 9th	12.10 p.m.	148		42		Very restless. Considerable dyspnea.
	1.40 p.m.	142				
	2.20 p.m.		Strophanthin 1/500 grain			
	2.55 p.m.	144				Went to sleep after injection.
	5 p.m.	136				Says that he "feels easier."
	5.20 p.m.		Strophanthin 1/500 grain			
	5.55 p.m.	134				Went to sleep after injection.
	8.5 p.m.	136				
	8.20 p.m.		Strophanthin 1/250 grain			
	9 p.m.	132				Went to sleep after injection.
	11.35 p.m.	134				
10th	9 a.m.	130		50	4-5½	Appearance improved. Slept all night. Breathing less distressed.
	9.20 a.m.		Strophanthin 1/250 grain			
	9.50 a.m.	118				
	12 noon.	104				
	12.20 p.m.		Strophanthin 1/500 grain			
	12.50 p.m.	106				Constantly sleeping during the day time.
	3.40 p.m.	112				
	5 p.m.	116				
	5.20 p.m.		Strophanthin 1/250 grain			Slight rise of temperature in evening (99.4° F.).
	6.10 p.m.	114				
	8.35 p.m.	110				
11th	9.10 a.m.	106		50	4-5¼	
	10 a.m.		Strophanthin 1/250 grain			
	10.40 a.m.	90				
	12 noon.	86				
	2 p.m.	88				Sudden pain in right knee at 11 p.m. Says it "feels numb," nothing abnormal on examination.
	5 p.m.	96				
12th	9 a.m.	106		48		Slept well. Foot easier.
	2.50 p.m.	108				Feels well.
	8.20 p.m.	104				
13th	9.25 a.m.	110		38		Slept well.
	8.55 p.m.	100				
14th	9.45 a.m.	98	Tr. Digit. m. 15	42	½-4½	Foot improving. Slept well.
15th	10.50 a.m.	88	Tr. Digit. m. 45	42	½-4½	
	8.35 p.m.	84				
16th	10.5 a.m.	80		60	½-4½	Slept well.
	8.50 p.m.	84	Tr. Digit. m. 45			
17th	8.50 a.m.	84	Tr. Digit. m. 45	62		
18th	9.55 a.m.	82		58		
	8.35 p.m.	78	Tr. Digit. m. 45			
19th	9.45 a.m.	80		68	½-5	Steadily improving. Slight pulsation in neck.
	9.5 p.m.	78	Tr. Digit. m. 45			
20th	9.55 a.m.	72		66	½-4½	Feels well.
	8.45 p.m.	74	Tr. Digit. m. 45			
21st	9.40 a.m.	74		76	½-4½	
	6.40 p.m.	70	Tr. Digit. m. 45			
22nd	9.45 a.m.	64		64		Very well. Sleeps and eats well.
	8.25 p.m.	62	Tr. Digit. m. 15 (Total 6½ drs.).			

DATE.	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
Sept. 23rd	9.45 a.m.	70		74	0-4 $\frac{1}{4}$	
	8.25 p.m.	66				
24th	11.10 a.m.	70				
	9.15 p.m.	70				
25th	9.40 a.m.	72		48		Up 2 hours.
	7.40 p.m.	78				
	8.30 p.m.	72				
26th	9.35 a.m.	70		44	$\frac{1}{2}$ 4 $\frac{1}{4}$	Up 2 hours. Condition remains the same.
	8.40 p.m.	62				
27th	9.40 a.m.	72		42	$\frac{1}{2}$ 4 $\frac{1}{4}$	Up 2 hours.
	8.45 p.m.	70				
28th	9.40 a.m.	76		46		Feels well.
	6.30 p.m.	84				Up 2 hours.
29th	9.40 a.m.	66		42	0-4 $\frac{3}{4}$	Up 2 hours.
	8.45 p.m.	82				
30th	9.35 a.m.	92		42	$\frac{3}{4}$ 4 $\frac{1}{4}$	Up 2 hours.
	8.10 p.m.	84				Walking in grounds in afternoon.
Oct. 1st	12.40 p.m.	78		42		Up 2 hours.
	9 p.m.	86				
2nd	9.45 a.m.	82		50	$\frac{3}{4}$ 4 $\frac{1}{4}$	Up all day.
	7.20 p.m.	96				Feels perfectly well.
3rd	9.35 a.m.	90		44	$\frac{3}{4}$ 4 $\frac{1}{4}$	
	8.25 p.m.	87				
4th	9.35 a.m.	88		54	$\frac{1}{2}$ 5	
	6.40 p.m.	94				
5th	9.35 a.m.	86		56	$\frac{1}{2}$ 5	
	8.20 p.m.	94				
6th	9.35 a.m.	90		50	$\frac{1}{2}$ 4 $\frac{1}{4}$	
7th	9.20 a.m.	88		54		
	8.35 p.m.	100				
8th	9 p.m.	90		52		
9th	10.15 a.m.	102		52	$\frac{1}{4}$ 4 $\frac{1}{4}$	
	9 p.m.	96				
10th	8.35 p.m.	106		54		
11th	10.35 a.m.	114		44	$\frac{1}{4}$ 4 $\frac{1}{4}$	
	8.10 p.m.	110				
12th	9.45 a.m.	106		46	$\frac{1}{4}$ 5 $\frac{1}{4}$	Feels very well. Up all day. Walking round grounds, climbing stairs, &c., but not able to do hard work yet. Discharged.

CASE 3. J. D., a man, aged 21. Auricular fibrillation. Mitral stenosis and incompetence. Fibroid disease of the apex of the right lung. Great improvement in general condition and reduction of the heart rate following the administration of strophanthin, on several different occasions.

Admitted on September the 5th, 1911, complaining of cough, pain in the left side of the chest, shortness of breath and a feeling of lassitude.

Family history. His father died of asthma and bronchitis. His mother, his five brothers and one sister are all well.

Previous illnesses. The patient had enjoyed good health until 1907, when he had an attack of rheumatic fever for which he received treatment in hospital for three months. At that time it was noted that the cardiac dulness extended 1 inch to the right of the sternum, the pulse was irregular and systolic and short presystolic bruits were present at the apex. In April, 1911, he suddenly began to suffer from shortness of breath, which became very much worse within two days. He was conscious of rapid and vigorous palpitation and he states that this was quite perceptible through his clothes. After these symptoms had been present for seven days he was readmitted to hospital. The following condition was noted. Apex beat in the sixth left inter-space. The cardiac dulness extended 3 inches to the right of mid-sternum at the level of the fourth space. Presystolic and systolic bruits were present at the apex and a systolic murmur was heard at the aortic base. There was impairment of the percussion note at the right apex and

vocal resonance was increased. Tubercle bacilli were not found in the sputum though it was examined on five different occasions. One milligramme of Old Tuberculin produced a violent reaction which lasted for three days. From June the 16th to July the 16th the patient was treated with increasing doses of tuberculin (bacillary emulsion) commencing with a dose of 1/1000 milligramme, and when a dose of 4/100 milligramme had been reached a reaction occurred. On May 30th tincture of digitalis was prescribed and the dose was gradually increased. On July the 27th the patient was taking 50 minims three times a day; on August the 7th this was reduced to 25 minims; on August the 23rd it was increased to 37 minims, and on August the 30th it was decreased to 20 minims three times daily. The heart and pulse rates were as follows:—

	May 5th	May 30th	June 10th	June 20th	July 1st
Apex ..	130	130	140	140	120
Radial ..	84	100	100	100	90
	July 10th	July 30th	August 10th	Sept. 1st.	
Apex ..	120	100	90	100	
Radial ..	90	90	84	84	

I am indebted to St. Bartholomew's Hospital for the above notes.

Condition on admission. His complexion is sallow, there is slight cyanosis of the lips and cheeks; the vessels at the root of the neck pulsate vigorously. The apex beat is in the sixth left interspace, $\frac{1}{2}$ an inch outside the nipple line. There is considerable pulsation of the left side of the chest with each heart beat. The deep cardiac dullness extends $5\frac{1}{2}$ inches to the left of the middle line. A rough diastolic bruit is present at the apex and a loud blowing systolic murmur, conducted round the axilla, is heard over the whole of the præcordial area. Both first and second sounds are very loud over the pulmonary area. The heart is rapid in rate and irregular in action. There are present impairment of resonance, prolongation of expiration, moist crackling rales, occasional rhonchi, whispering pectoriloquy over the apex of the right lung and oedema of the base of the left lung. The liver is not enlarged and there is no oedema of the feet. The urine contains a trace of albumen and scanty granular casts. Polygraphic records show complete irregularity of the heart's action and the ventricular form of venous pulse.

Treatment and progress. There was no alteration in the patient's condition after ten days rest in bed. The patient received 15 minims of tincture of digitalis on September the 14th and again on the 15th. A rough thrill, diastolic in time, was palpable at the apex on this latter date. On September the 18th 1/500 grain of strophanthin was given at 10.30 a.m. and 1/250 grain at 1.40 p.m. in consequence of which the heart rate fell from 130 to 93 per minute during a period of four hours. At the same time the pulsation at the root of the neck became less and the patient's condition improved. On September the 20th he stated that he had not felt so well since the commencement of his illness. The ventricular rate rose to 114 per minute by September the 23rd, when a single injection of 1/250 grain produced a fall in rate from 114 to 84 per minute in $5\frac{1}{2}$ hours. There was slight oedema of the base of the right lung on September the 29th. His condition improved, and, though the pulse gradually accelerated, he remained well until October the 4th when he complained of feeling ill and of a sore throat, but nothing definite was made out on examination. He was pale, restless, and vomiting; there was considerable dyspnoea and the ventricular rate was rapid (174 per minute). On the evening of October the 5th he became very much worse (ventricular rate 184 per minute). Two injections of strophanthin of 1/250 grain each were given at 6.50 p.m. and 8.50 p.m. respectively, with a result that the heart rate fell to 96 per minute by 9.30 a.m. on the 6th of October. Fig. 3 illustrates this fall of rate. There was pain at the site of both injections which lasted from one to two hours, after which he fell asleep and slept all night. On October the 6th a further injection of 1/250 grain was given at 10.15 a.m. and the heart rate fell to 76 per minute in $4\frac{3}{4}$ hours. The bruit which had previously filled diastole now became early diastolic. The urine increased in amount during the next few days. From October the 6th to the 25th he remained in good health, but the heart rate gradually rose and it was 118 per minute on the latter date. On October the 25th four injections of 1/500 grain each were given at intervals of one hour but their effect was slight. His condition remained unchanged, though the heart steadily increased in rate, until November the 10th when palpitation and dyspnoea again showed themselves. His complexion was sallow; there was considerable pulsation in the neck and epigastrium, with heaving of the left side of the chest at each heart beat; the liver was palpable two fingerbreadths below the right costal margin and there was vomiting associated with pain and tenderness in the epigastrium. Tincture of digitalis in 15 minim doses given four times daily was commenced on November the 11th but was discontinued after the 16th owing to gastric disturbances. The heart rate during this time had fallen from 154 to 80 per minute and a total of 6 drachms of digitalis had been taken. The effect of the digitalis on the ventricular rate was noticeable on the first day of administration and an increase in the flow of urine took place. After November the 17th the ventricular rate gradually increased until on December the 8th palpitation, vomiting, dyspnoea and pulsation in the neck returned. Tincture of digitalis in 15 minim doses given four times daily was prescribed with prompt amelioration of the symptoms. At no time was any alteration in the extent of cardiac dullness observed. The condition of auricular fibrillation, as shown by polygraphic tracings, persisted throughout the period of observation. The patient was discharged on December the 30th greatly improved. Fig. 8 illustrates in this case the gradual increase of rate and the abrupt fall which occurred on the administration of strophanthin.

TABLE IV. (CASE 3.)

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	REMARKS.
Sept.					
8th		116		28	
11th	12.15 p.m.	118		43	
12th	8.25 p.m.	110		44	
13th	12.15 p.m.	100		43	
	9 p.m.	94			
14th	9.40 a.m.	108	Tr. Digit. m. 15	38	Slight cyanosis of lips and cheeks. Sleeps and eats well. Breathing not distressed.
15th	11.15 a.m.	134	Tr. Digit. m. 15	38	Slight pulsation in vessels of neck.
	8.40 p.m.	98			
16th	10.15 a.m.	114		46	Slept well. Pulsation in neck well marked.
	8.55 p.m.	96			
17th	8.55 a.m.	120		58	
18th	9.55 a.m.	130		56	Cough troublesome. Conspicuous pulsation in neck. Not feeling well.
	10.30 a.m.		Stroph. 1/500 gr.		
	11 a.m.	120			
	11.30 a.m.	112			
	12 noon	106			
	12.30 p.m.	108			
	1 p.m.	104			
	1.40 p.m.		Stroph. 1/250 gr.		
	2.5 p.m.	108			
	2.30 p.m.	93			
	3 p.m.	96			
	3.30 p.m.	94			
	4.30 p.m.	92			
	6.30 p.m.	94			
	8.30 p.m.	98			
19th	9.30 a.m.	106		66	Feels better. Cough less. Pulsation at root of neck less conspicuous.
	9 p.m.	102			
20th	10 a.m.	106		60	Improved. Says he "feels better than he has felt for five months."
	8.45 p.m.	92			
21st	9.30 a.m.	106		50	
	6.40 p.m.	104			
22nd	9.40 a.m.	104			Feels well. Pulsation in neck still present.
	8.30 p.m.	90			
23rd	9.5 a.m.	114	Stroph. 1/250 gr.	60	
	9.43 a.m.				
	10.15 a.m.	102			Pulsation diminished after injection.
	11.20 a.m.	100			
	12.20 p.m.	90			
	1.15 p.m.	90			
	2.20 p.m.	92			
	3.20 p.m.	84			
	8.20 p.m.	88			
24th	11.15 a.m.	92		48	
	9.20 p.m.	90			
25th	9.45 a.m.	94		46	
	8.35 p.m.	84			
26th	9.40 a.m.	120		44	
	8.40 p.m.	76			
27th	9.45 a.m.	94		52	
	8.50 p.m.	78			
28th	9.45 a.m.	102		48	Feeling well. Looks well.
	6.30 p.m.	104			
29th	9.45 a.m.	120		46	
	8.50 p.m.	90			
30th	9.30 a.m.	104		42	
	8.15 p.m.	102			

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	REMARKS.
Oct.					
1st	12.45 p.m.	114		46	
	9 p.m.	100			
2nd	9.50 a.m.	126		50	
	7.15 p.m.	94			
3rd	9.40 a.m.	144		48	
	8.30 p.m.	104			
4th	9.30 a.m.	174		50	Feels ill. Pale. Restless. Dyspnoea. Vomiting. Complains of sore throat.
	6.35 p.m.	118			
5th	9.30 a.m.	117		62	
	6.15 p.m.	184			Looks very ill. Dyspnoea has increased. Very restless and sleepless.
	6.50 p.m.		Stroph. 1/250 gr.		
	7 p.m.	160			
	7.15 p.m.	174			Pain at site of injection.
	7.30 p.m.	174			
	7.45 p.m.	162			
	8 p.m.	150			
	8.15 p.m.	162			
	8.30 p.m.	158			
	8.45 p.m.	142			
	8.50 p.m.		Stroph. 1/250 gr.		
	9 p.m.	132			Pain at site of injection.
	9.15 p.m.	136			
	9.30 p.m.	132			
	9.45 p.m.	132			
	10 p.m.	138			
	10.15 p.m.	156			
	10.30 p.m.	156			
	10.45 p.m.	148			
	11 p.m.	126			
	11.15 p.m.	122			
	11.30 p.m.	138			
	11.45 p.m.	140			
6th	9.30 a.m.	96		38	Sleeping. Greatly improved.
	10.15 a.m.		Stroph. 1/250 gr.		
	10.30 a.m.	94			
	10.45 a.m.	92			
	11 a.m.	88			
	11.15 a.m.	86			
	11.30 a.m.	84			
	11.45 a.m.	84			
	12 noon.	86			
	12.15 p.m.	84			
	12.40 p.m.	80			
	1.10 p.m.	90			
	1.40 p.m.	80			
	2.30 p.m.	78			
	3 p.m.	76			
	3.30 p.m.	86			
	4 p.m.	84			
	4.30 p.m.	86			
	5.5 p.m.	86			
	5.30 p.m.	90			
	6 p.m.	76			
7th	9.15 a.m.	84		40	
	8.40 p.m.	74			
8th	9.10 p.m.	70		34	
9th	10.5 a.m.	74		50	
	9.5 p.m.	70			
10th	8.35 p.m.	70		52	
11th	10.30 a.m.	90		60	
	8.15 p.m.	76			

DATE	HOUR AT WHICH FRACING TAKEN.	HEART RATE PER MIN.	DRUG	URINE (IN OZS.)	REMARKS.
Oct.					
12th	9.50 a.m.	100		54	
	9.25 p.m.	88			
13th	11 a.m.	98		44	
	9.25 p.m.	80			
14th	12.10 p.m.	88		56	Up 2 hours. Feels well.
	8.15 p.m.	84			
15th	12 noon	94		42	Up 2 hours.
	9.5 p.m.	86			
16th	8.55 p.m.	86			Up 2 hours.
17th	10.5 a.m.	110		34	Up 2 hours.
	8.15 p.m.	88			
18th	11 a.m.	112		36	Up 2 hours.
19th	10.10 a.m.	126		34	Up 2 hours.
	8.20 p.m.	104			
20th	10 a.m.	132		22	Some pulsation in neck.
	8 p.m.	124			Up 3 hours.
21st	10.10 a.m.	110		26	Up 3 hours.
	8.30 p.m.	114			
22nd	1.5 p.m.	164		26	Marked pulsation in neck and in left side of chest. Orthopnoea and vomiting. Restless. Red.
	9.20 p.m.	130			
23rd	9.30 a.m.	122		22	
	8.15 p.m.	158			
24th	10 a.m.	136		26	Feels ill. Same symptoms as on 22nd.
	8.30 p.m.	128			
25th	9.15 a.m.	118		40	
	9.30 a.m.	112			
	9.45 a.m.	122			
	9.52 a.m.		Stroph. 1/500 gr.		
	10 a.m.	120			
	10.15 a.m.	116			
	10.30 a.m.	104			
	10.45 a.m.	118			
	11 a.m.		Stroph. 1/500 gr.		
	11 a.m.	122			Pain after injection.
	11.15 a.m.	122			
	11.30 a.m.	138			
	11.45 a.m.	140.			
	11.52 a.m.		Stroph. 1/500 gr.		
	12 noon	126			Pain after injection.
	12.15 p.m.	124			Hyperæsthesia and redness down outer edge of right forearm.
	12.30 p.m.	122			
	12.45 p.m.	140			
	12.55 p.m.		Stroph. 1/500 gr.		
	1 p.m.	128			Pain after injection.
	1.15 p.m.	120			Redness and hyperæsthesia along inner side of left forearm.
	1.30 p.m.	118			
	1.50 p.m.	110			
	2 p.m.	112			
	2.15 p.m.	114			
	2.30 p.m.	118			
	3 p.m.	122			
	4.45 p.m.	108			
	5 p.m.	112			
	6.15 p.m.	104			
	6.50 p.m.	102			
	7.15 p.m.	100			
26th	10 a.m.	100		32	Feeling better.
	1.45 p.m.	110			Appearance improved.
	8.35 p.m.	88			

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG	URINE (IN OZS.)	REMARKS
Oct.					
27th	10.35 a.m.	96		40	Feels well.
	6 p.m.	94			
28th	10.10 a.m.	106		38	
	6.45 p.m.	94			
29th	6.35 p.m.	96		34	
30th	10.10 a.m.	112		36	Up 2 hours.
	6 p.m.	104			
	8 p.m.	98			
31st	10 a.m.	108		26	Up 2 hours.
	8.10 p.m.	98			
Nov.					
1st	10.5 a.m.	102		22	Up 2 hours.
	8.50 p.m.	90			
2nd	10.15 a.m.	92		34	Up 2 hours.
	8.45 p.m.	82			
3rd	10.40 a.m.	114		34	Up 2 hours.
	8.25 p.m.	94			
4th	9.35 a.m.	120		38	Up 2 hours.
	8.15 p.m.	88			
5th	2 p.m.	118		28	Up 4 hours.
	9.15 p.m.	90			
6th	10.5 a.m.	124		32	Up 4 hours.
	8 p.m.	98			
7th	8.5 p.m.	120		30	Up 4 hours.
8th	10.5 a.m.	130		38	Up 4 hours.
	9.5 p.m.	114			
9th	10 a.m.	168		36	Up 4 hours. Not so well.
	8.5 p.m.	146			Vomited.
10th	10.10 a.m.	144		36	Bed. Vomited. Dyspnœa.
	2 p.m.	158			Restless. Sallow complexion.
	6 p.m.	152			Pain in abdomen. Anorexia.
11th	10 a.m.	154		32	Dyspnœa. Felt better in the evening.
	2.15 p.m.	154			
	6 p.m.	128	Tr. Digit. 1 dr.		
12th	2 p.m.	104		50	Improved condition.
	9.15 p.m.	90	Tr. Digit. 1 dr.		Less restless.
13th	10 a.m.	96		48	
	2 p.m.	94			
	6 p.m.	82	Tr. Digit. 1 dr.		
14th	11.10 a.m.	86		48	
	8 p.m.	76	Tr. Digit. 1 dr.		
15th	10 a.m.	92		50	
	6 p.m.	78	Tr. Digit. 1 dr.		
16th	10.10 a.m.	90		44	Feels very well. Looks well.
	8.30 p.m.	80	Tr. Digit. 1 dr. (Total=6 drs.)		
17th	10 a.m.	90		46	Vomited.
	8.30 p.m.	68			
18th	10.5 a.m.	84		42	Up 2 hours.
	2 p.m.	80			
	8 p.m.	82			
19th	5.40 p.m.	86		46	Up 2 hours.
20th	10 a.m.	98		46	Up 2 hours.
	8.15 p.m.	100			
21st	10 a.m.	112		48	Up 2 hours.
	8.40 p.m.	100			
22nd	10.5 a.m.	136		42	Up 2 hours.
	5.50 p.m.	116			
23rd	10 a.m.	104		48	Up 4 hours.
	8.15 p.m.	108			
24th	10 a.m.	92		48	Up 4 hours.
	8.30 p.m.	90			
25th	10.15 a.m.	92		46	Up 4 hours.
	8 p.m.	92			

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	REMARKS
Nov.					
26th	2 p.m.	126		40	Up 4 hours.
	9.30 p.m.	90			
27th	10 a.m.	92		36	Up 4 hours.
	6.15 p.m.	108			
28th	10 a.m.	98		34	Up 4 hours.
	8 p.m.	100			
29th	10.15 a.m.	102		38	Up 4 hours.
	7.50 p.m.	104			
30th	10.15 a.m.	102		46	Up 4 hours.
	8.45 p.m.	102			
Dec.					
1st	11 a.m.	112		42	Up 5 hours.
	8.10 p.m.	166*			*Patient died in next bed.
2nd	11.30 a.m.	102		46	Up 5 hours.
3rd	9.20 a.m.	106		47	Up 5 hours.
4th	10.10 a.m.	98		44	Up 5 hours.
	8.15 p.m.	146			
5th	10 a.m.	108		40	Up 5 hours.
	8 p.m.	126			
6th	10 a.m.	106		40	Up 5 hours. Not feeling well.
	8.20 p.m.	132			Pain in epigastrium.
7th	10 a.m.	118		40	Up 5 hours.
	8.10 p.m.	132			
8th	11 a.m.	110		42	Palpitation and dyspnoea.
	9 p.m.	114	Tr. Digit. 1 dr.		Up 5 hours.
9th	10 a.m.	98		44	Feeling better.
	8.5 p.m.	110	Tr. Digit. 1 dr.		Up 5 hours.
10th	9.30 p.m.	74	Tr. Digit. 1 dr.	40	Up 5 hours.
11th	10.10 a.m.	82		42	Feeling well. Up 6 hours.
	7.50 p.m.	84	Tr. Digit. 1 dr.		
12th	10.15 a.m.	74		48	Up 6 hours.
	8.10 p.m.	78	Tr. Digit. 1 dr.		
13th	10.10 a.m.	76		50	Up 6 hours.
	8.10 p.m.	72	Tr. Digit. 1 dr.		Feels well.
14th	10.15 a.m.	70		58	Up 6 hours.
	9.30 p.m.	64	Tr. Digit. 1 dr.		
15th	10.5 a.m.	66		52	Up 6 hours.
	7.45 p.m.	74	Tr. Digit. 1 dr.		
16th	10.15 a.m.	68		50	Up 6 hours.
	8.25 p.m.	70	Tr. Digit. 1 dr.		
17th	7.40 p.m.	78	Tr. Digit. 1 dr.	56	Up 6 hours.
18th	10.15 a.m.	70	Tr. Digit. 15 m. (Total = 10 drs., 15 minims)	40	Up 6 hours.
19th	10 a.m.	68		38	Up 6 hours.
	8 p.m.	70			
20th	10 a.m.	80		42	Up 6 hours.
	8.15 p.m.	84			

Discharged on December the 30th, 1911.

CASE 4. E. B., a woman, aged 64. Auricular fibrillation. Arterio and cardio sclerosis. Slight and transient slowing of the heart rate after the administration of strophanthin.

Admitted on August the 3rd, 1911, complaining of breathlessness, and swelling of the feet

Family history. Her father died of "paralytic fits." Her mother, six brothers and two sisters are dead, but there is no history as to the causes of their deaths. Three sisters are alive and well.

Previous illnesses. The patient has had bronchitis every winter for several years and has suffered from "rheumatism" for many years, but there is no history of acute rheumatism. She has had shortness of breath for one week.

Condition on admission. There is considerable dyspnoea, which is increased by the slightest exertion. Her complexion is very sallow and the vessels of the cheeks are injected. She has a slight cough but only scanty expectoration. The deep cardiac dullness extends $4\frac{1}{2}$ inches to the left of the middle line. The action of the heart is irregular and an indistinct systolic murmur is present at the apex and at the tricuspid orifice. The pulmonic second sound is accentuated. The pulse is very poor in force and volume and the radial arteries at the wrist are thickened. The lungs are emphysematous and there is oedema of both bases. The liver is palpable one finger-breadth below the right costal margin. There is neither ascites nor oedema of the feet. The urine is scanty and contains a trace of albumen. Polygraphic tracings showed the ventricular form of venous pulse and gross irregularity of the heart beat.

Treatment and progress. The patient remained at rest in bed for nine days, but her condition did not improve. On August the 12th, 1 500 grain of strophanthin was given at 10.33 a.m. but only produced a slight effect on the heart rate. At 5.5 p.m. the dose was repeated, but the effect was slight. On August the 13th, an injection of 1 500 grain was given at 10.33 a.m. and again the result was slight, but the total effect of the three injections was to lower the heart rate from 124 to 94 per minute. Rises of temperature occurred on the evenings of August the 13th (100.4° F.) and the 14th (99.6° F.). There was no alteration in the symptoms nor physical signs on examination, on August the 10th and the 17th. From August the 13th to the 18th the heart rate remained at a lower level than previous to the administration of the strophanthin. On August the 18th, 1 500 grain of strophanthin was injected at 10.50 a.m., but with only a temporary effect on the heart rate. At 10.15 a.m. on August the 19th, 1 500 grain was injected, with the result that the heart rate increased and within thirty minutes of a second injection of 1 500 grain, given at 2.55 p.m., it had risen from 114 to 136 per minute. At 6.40 p.m. it was 132 per minute but had fallen to 116 per minute by 10.20 a.m. on August the 20th. There were sharp rises of temperature on the evenings of August the 19th (101° F.) and the 20th (100.6° F.). Tincture of digitalis in 15 minim doses, three times daily, was prescribed on August the 21st, but was discontinued on August the 28th, when the patient had taken $5\frac{1}{2}$ drachms. During this period the heart rate gradually fell from 118 to 74 per minute. From August the 25th to the 28th the flow of urine increased and reached a maximum of 64 ounces on the latter date. The condition of the patient had improved, but owing to the persistent sleeplessness, chloral and potassium bromide were ordered on two occasions. During the night of August the 31st the patient complained of "cramp" of the left foot and she stated that "it felt like a lump of lead." Examination revealed no impairment of sensation nor any signs of obstruction to the blood flow. Cheyne-Stokes breathing was present and there was oedema of the bases of the lungs. After this the ventricular rate gradually increased and reached 126 per minute on September the 11th. On September the 12th an injection of 1 250 grain of strophanthin was given at 9.55 a.m., the ventricular rate being 110 per minute, and this dose was repeated at 2.10 p.m. with a result that the ventricular rate dropped to 94 per minute by 8.15 p.m. The temperature rose to 102.2 degrees Fahr. on the evening of September the 13th. On September the 14th the patient felt better, but there was oedema of both feet, of the right leg, and of the bases of both lungs. The respirations were rapid but the Cheyne-Stokes breathing had disappeared. As the ventricular rate did not remain slow tincture of digitalis, in 15 minim doses three times daily, was prescribed with a diuretic mixture on September the 14th. The heart rate gradually fell and on September the 25th it was 80 per minute; it remained at this rate until October the 14th, when the digitalis was discontinued, a total of $22\frac{1}{2}$ drachms having been taken. Theocin sodium acetate in 7 grain doses was added to the digitalis on September the 28th, but the increase in urine was very slight in amount. On this date there was extensive oedema of the legs, up to the sacrum, and of the bases of the lungs. Cheyne-Stokes breathing was present. On October the 12th there was oedema of the bases of both lungs. The patient left hospital on October the 16th, but for several days previously she had shown evidences of mental change. The Cheyne-Stokes breathing persisted to the date of her discharge. Polygraphic tracings exhibited gross irregularity of the heart's action and the ventricular form of venous pulse throughout the whole period of observation.

TABLE V. (CASE 4.)

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG	URINE (IN OZS.)	REMARKS.
Aug.					
3rd	8.15 p.m.	118			Dyspnoea. Sallow complexion.
5th	9 p.m.	102		21	
7th	12 noon.	140		24	
9th	12 noon.	116		22	
11th		132		22	
12th	9 a.m.	124		20	
	10.33 a.m.		Stroph. 1/500 gr.		
	11.5 a.m.	114			

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	REMARKS.
Aug.					
12th	11.40 a.m.	124			
	12.30 p.m.	114			
	2.30 p.m.	108			
	4.30 p.m.	118			
	5.5 p.m.		Stroph. 1/500 gr.		
	5.35 p.m.	114			
	7 p.m.	112			
	9 p.m.	114			
13th	9.30 a.m.	103		24	Feels better.
	10.33 a.m.		Stroph. 1/500 gr.		Rise of temperature in the evening (100.4° F.).
	11.5 a.m.	103			
	12.30 p.m.	106			
	2 p.m.	94			
	6.30 p.m.	110			
14th	10.20 a.m.	88		29	Rise of temperature in the evening (99.6° F.).
	8.20 p.m.	104			
15th	9.30 a.m.	108		33	
	8.30 p.m.	98			
16th	9.30 a.m.	94		28	
	9.20 p.m.	114			
17th	9.40 a.m.	108		42	
18th	9.45 a.m.	104		31	
	10.50 a.m.		Stroph. 1/500 gr.		
	11.20 a.m.	102			
	1.55 p.m.	102			
	3.35 p.m.	96			
	6.50 p.m.	114			Sleepless.
19th	9.25 a.m.	100		33	Rise of temperature to 101 deg. F. in the evening.
	10.15 a.m.		Stroph. 1/500 gr.		
	10.45 a.m.	112			Chloral, grains 10.
	2 p.m.	114			Pot. Brom. grains 30 at night.
	2.55 p.m.		Stroph. 1/500 gr.		
	3.35 p.m.	136			
	6.40 p.m.	132			No improvement.
20th	10.20 a.m.	116		26	Rise of temperature in the evening (100.6° F.).
21st	8.45 p.m.	118	Tr. Digit. m. 15	40	
22nd	9.50 a.m.	106		31	
	9 p.m.	86	Tr. Digit. m. 45		
23rd	9.10 p.m.	98	Tr. Digit. m. 45	39	
24th	8.30 p.m.	93	Tr. Digit. m. 45	32	
25th	8.50 p.m.	78	Tr. Digit. m. 45	36	
26th	8.55 p.m.	84	Tr. Digit. m. 45	42	
27th	10.15 a.m.	72	Tr. Digit. m. 45	46	
28th	9.35 a.m.	74	Tr. Digit. m. 30	64	
		(Total taken = 5½ drachms)			
30th	9.45 a.m.	84		32	Slept well. Feels better.
	8.30 p.m.	88			
31st	9.45 a.m.	66		44	Sleep broken.
	9 p.m.	102			
Sept.					
1st	12 noon	86		42	Slept fairly well. Cramp in left foot. Cheyne-Stokes breathing present.
	9.5 p.m.	94			
2nd	9.30 a.m.	82		36	Feels a little better.
3rd	9.35 a.m.	82		28	Slept well
4th	10 a.m.	86		24	Foot feels numb.
5th	9.40 a.m.	92		21	
6th	9.50 a.m.	92		16	Slept well. Foot in same condition.
	9.40 p.m.	104			
7th	11 a.m.	104		35	Very little sleep last night.
	9 p.m.	108			Not so well.
8th	9.30 a.m.	105		21	

DATE	HOOR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	REMARKS.
Sept.					
9th	9.35 a.m.	100		20	Slept well. Feels much better, Breathing easier.
11th	12.30 p.m.	110		24	Dyspnoea. Sleepless. Cheyne-Stokes breathing.
12th	9.30 p.m.	126			
	9.10 a.m.	110		18	Very little sleep last night.
	9.55 a.m.		Stroph. 1 250 gr.		Orthopnoea.
	10.30 a.m.	122			
	1.30 p.m.	102			Chloral, grains 10.
	2.10 p.m.		Stroph. 1/250 gr.		Pot. Brom. grains 30 at night.
	2.40 p.m.	92			Evening temperature 100° F.
	5.15 p.m.	112			
	8.15 p.m.	94			
13th	11.50 a.m.	102		34	Feels better. Evening temperature 102.2° F.
	9.5 p.m.	116			
14th	10.55 a.m.	106	Tr. Digit. m. 45	34	Digitalis combined with diuretic mixture. Oedema of both feet and right leg.
15th	9.35 a.m.	98		26	
	8.50 p.m.	108	Tr. Digit. m 45		Breathing easier.
16th	10.20 a.m.	102		15	Dyspnoea. Sleepless.
	9 p.m.	120	Tr. Digit. m. 45		
18th	8.40 p.m.	111	Tr. Digit. m. 45	26	
19th	9.55 a.m.	112		16	Cheyne-Stokes breathing marked.
	8.50 p.m.	98	Tr. Digit. m. 45		Pain in left side.
20th	10.15 a.m.	104		12	Cheyne-Stokes breathing present.
	8.50 p.m.	117	Tr. Digit. m. 45		Pleural rub at base of left lung.
21st	11.20 a.m.	99		30	
	6.45 p.m.	102	Tr. Digit. m. 45		
22nd	12.10 p.m.	94		20	Breathing difficult.
	8.15 p.m.	108	Tr. Digit. m. 45		Pain in left foot.
23rd	10.15 a.m.	94		24	Feels a little better.
	8.50 p.m.	100	Tr. Digit. m. 45		
24th	9.25 p.m.	96	Tr. Digit. m. 45	16	
25th	12 noon	80		18	
	8.40 p.m.	92	Tr. Digit. m. 45		
26th	9.30 a.m.	80	Tr. Digit. m. 45	24	
	8.45 p.m.	75			
27th	8.55 p.m.	92	Tr. Digit. m. 45	12	Somewhat improved.
28th	9.35 a.m.	90	Tr. Digit. m. 45	30	Theocin sodium acetate grains 7 added to each dose of digitalis.
	6.35 p.m.	80			
29th	9.50 a.m.	80	Tr. Digit. m. 45	38	
	8.55 p.m.	78			
30th	10.5 a.m.	84	Tr. Digit. m. 45	28	
	8.30 p.m.	94			
Oct.					
1st	11.20 a.m.	86	Tr. Digit. m. 45	58	
	9.5 p.m.	88			
2nd	10 a.m.	82	Tr. Digit. m. 45	46	
	7.30 p.m.	82			
3rd	12.35 p.m.	86	Tr. Digit. m 45.	34	Oedema diminishing.
	8.35 p.m.	86			Sleeping better.
4th	12 noon	80	Tr. Digit m. 45	18	
	6.45 p.m.	88			
5th	9.45 a.m.	74	Tr. Digit. m. 45	46	
	8.30 p.m.	78			
6th	9.50 a.m.	82	Tr. Digit. m. 45	36	
7th	12 noon	88	Tr. Digit. m. 45	40	
	8.20 p.m.	80			

Discharged on October the 16th

CASE 5. A. P., a woman aged 49. *Auricular fibrillation. Mitral and aortic disease. Reduction of heart rate and improvement in symptoms following the use of strophanthin; sudden death 12 hours after the last injection.*

Admitted on September the 28th, 1911, complaining of shortness of breath, sleeplessness and nausea after meals.

Family history. No history obtainable.

Previous illnesses. The patient had never had acute rheumatism. For some years she had had attacks of fainting with pain over the præcordial area. These attacks have been worse during the two years preceding admission. There has been oedema of the feet since August.

Condition on admission. The patient sits propped up in bed, her breathing is laboured, respiration 22 per minute, and she is very restless. Her complexion is sallow and her cheeks, nose, and the lips are cyanosed. There is considerable pulsation of the vessels at the root of the neck even when the patient stands. Her finger tips are slightly clubbed. There is pulsation over the left side of the chest. The apex beat is in the sixth left interspace in the anterior axillary line and a slight thrill is detected here on palpation. The deep cardiac dulness extends $1\frac{1}{2}$ inches to the right and 6 inches to the left of the mid-sternum. The action of the heart is very rapid (180 per minute) and very irregular. At the apex an indistinct bruit is present, which is difficult to time owing to the rapidity and irregularity of the heart's action. The second sound in the mid-axillary line and at the pulmonic area is accentuated. The liver is palpable four fingerbreadths below the right costal margin. There is oedema of the bases of both lungs, the feet, legs, and over the sacrum, and there is some ascites. The veins of the legs are varicose. There are present gross irregularity of the heart's action and the ventricular form of venous pulse as shown by polygraphic tracings.

Treatment and progress. The patient remained at rest in bed for five days. On October the 3rd a single injection of 1.250 grain of strophanthin was given at 10.14 a.m. the heart rate being 178 per minute, and it fell to 134 per minute in 24 hours, and at the same time an amelioration of the symptoms took place, though the patient still continued sleepless. On October the 7th her condition remained unaltered. At 12.22 p.m. 1.250 grain of strophanthin was injected, when the heart rate was 160 per minute, and another injection of 1.250 grain was given at 3.22 p.m. followed three hours later by an injection of 1.500 grain. At 7 p.m. the heart rate had fallen to 76 per minute, a fall of 84 beats per minute in $6\frac{1}{2}$ hours. The patient felt more comfortable, her breathing was easier, her appearance had improved and she slept on one or two occasions while tracings were taken. The ventricular rate remained about 90 per minute during the last two hours during which tracings were taken. She slept well during the night. At 5 a.m. on the following morning (October the 8th), while sitting up in bed talking, she suddenly complained of a pain in her abdomen and a few minutes later dropped back dead. At no time was any undue slowing of the heart observed. The ventricular form of venous pulse and the gross irregularity of the heart beat persisted throughout the period of observation. Fig. 4, which is compiled from tracings taken from this patient, shows the abrupt fall of rate occurring after the administration of strophanthin.

TABLE VI. (CASE 5.)

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG	URINE (IN OZS.)	SIZE (IN INCHES)	REMARKS.
Sept. 28th	3.30 p.m.	180			$1\frac{1}{2}$ 6	Cyanosis of lips and cheeks. Orthopnoea. Oedema of feet.
	6.10 p.m.	176				
29th	10 a.m.	160		26		
	2 p.m.	154				
	6 p.m.	154				
30th	10 a.m.	164		32		
	2 p.m.	168				
	6 p.m.	168				
Oct. 1st	11.15 a.m.	170		21		
	6 p.m.	176				
2nd	10 a.m.	158		30		
	2 p.m.	168				
	6.20 p.m.	172				
3rd	9.30 a.m.	170		44		Marked pulsation on neck present even when standing. Poor appetite. Feels sick after meals. Restless and sleepless at night. Cyanosis of lips and cheeks. Orthopnoea.

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES)	REMARKS.
Oct. 3rd	10.14 a.m.	178	Stroph. 1/250 gr.			
	10.14 a.m.					
	10.30 a.m.	176				
	10.45 a.m.	166				
	11 a.m.	172				Slept while tracing taken
	11.15 a.m.	168				
	11.30 a.m.	154				
	11.45 a.m.	168				
	12 noon	162				
	12.15 p.m.	156				
	12.30 p.m.	153				
	1 p.m.	162				
	1.30 p.m.	152				
	2 p.m.	152				
	3 p.m.	148				
	3.30 p.m.	156				
	4 p.m.	148				
	4.30 p.m.	156				
	5 p.m.	154				
	5.30 p.m.	148				Dyspnoea slightly less evident.
4th	6 p.m.	164				
	10 a.m.	134		10		Pulse slightly slower. Feels better.
	6 p.m.	160				Slept badly last night.
5th	9.50 a.m.	166		37		
	6.5 p.m.	146				
6th	9.55 a.m.	146		21		
	6 p.m.	132				
7th	9.10 a.m.	158		16	2 1/2 - 7 1/2	Dyspnoea still present but not so great as on admission.
	12 noon	160	Stroph. 1/250 gr.			
	12.22 p.m.					
	12.30 p.m.	146				
	12.45 p.m.	132				
	1 p.m.	140				
	1.15 p.m.	146				
	1.30 p.m.	140				
	1.45 p.m.	136				
	2 p.m.	136				
	2.15 p.m.	130				
	2.30 p.m.	138				
	2.45 p.m.	134				
	3 p.m.	144				
	3.15 p.m.	150				
	3.22 p.m.					
	3.30 p.m.	130				
	3.45 p.m.	110				
	4 p.m.	108	Stroph. 1/500 gr.			
	4.15 p.m.	120				
	4.30 p.m.	114				
	4.45 p.m.	106				
	5 p.m.	102				
	5.15 p.m.	106				
	5.30 p.m.	112				
	5.45 p.m.	100				
	6 p.m.	96				
	6.15 p.m.	90				
	6.25 p.m.					
	6.30 p.m.	90				
	6.45 p.m.	82				Feeling very much better.
	7 p.m.	76				
	7.15 p.m.	86				
	7.30 p.m.	88				
	7.45 p.m.	82				
	8 p.m.	86				

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
Oct.						
7th	8.15 p.m.	82				
	8.30 p.m.	86				
	8.45 p.m.	76				
	9 p.m.	88				Sleeping.
	9.15 p.m.	88				Sleeping.
8th	5.45 a.m.					Died unexpectedly.

Post Mortem Examination

Post mortem rigidity well marked. Post mortem staining in dependent parts. Oedema of the right foot and leg. The right pleural cavity contained 34 ounces and the left 2 ounces of a clear serous fluid. The right lung weighed 20 ounces and the left 16 ounces; both were oedematous. The peritoneal cavity contained 12 ounces of a clear serous fluid. The liver weighed 52 ounces. Its surface was rough and its substance hard. There was an adhesion $2\frac{1}{2}$ inches long and 2 inches wide between the upper and outer surface of the right lobe of the liver and the under surface of the diaphragm. On section the organ presented a "nutmeg" appearance. The spleen weighed 5 ounces, was hard, and there was some perisplenitis. The right kidney weighed $5\frac{3}{8}$ ounces. Its capsule was slightly adherent around the hilum. The left kidney weighed $6\frac{1}{8}$ ounces and the capsule was adherent round the hilum. On section both kidneys presented a congested appearance. There was a small fibroid tumour at the fundus of the uterus. The heart, pericardium and roots of the vessels weighed, in all, 32 ounces. The pericardial sac contained 6 ounces of a clear serous fluid. There were no pericardial adhesions, but a small milk-white spot was present at the apex of the left ventricle. There was no clot in the pulmonary artery. The wall of the left ventricle was considerably hypertrophied and the wall of the right ventricle also but to a less extent. The flaps of the mitral valve and aortic cusps were much thickened.

CASE 6. A. J., a man, aged 29. *Paroxysmal tachycardia (non-rheumatic)*. Showing of the rate of paroxysm with continuation of the fibrillation for nine days after the administration of strophanthin.

Admitted on October the 13th, 1911, in a paroxysm of tachycardia. At 1 p.m. he was suddenly attacked with palpitation, dyspnoea, vomiting and collapse.

Family history. His mother died of "heart trouble" at the age of 57. He has two brothers and two sisters, all of whom are healthy.

Previous illnesses. He had good health until $2\frac{1}{2}$ years ago, since when he has been subject to attacks similar to that on admission. There is no history of rheumatism or chorea. Full details of the past history of this case are given in *Heart*, 1912, iii, 173, CASE I.

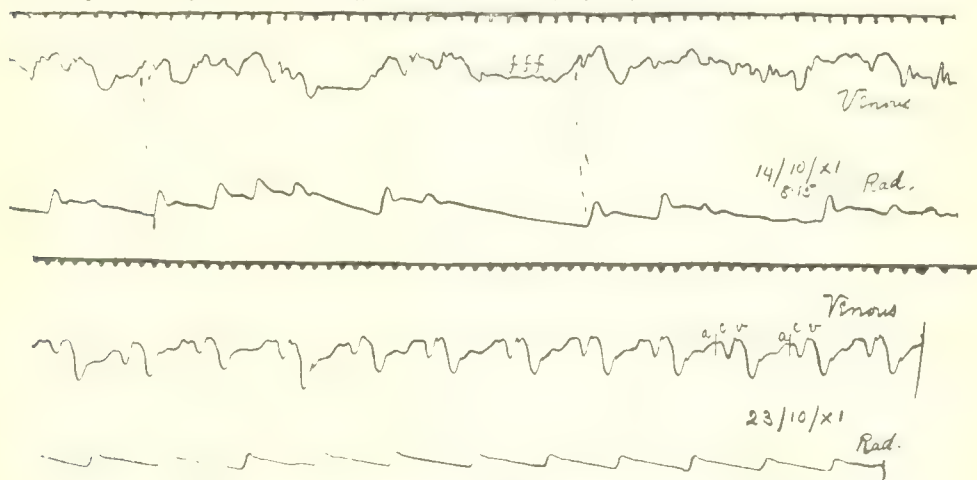


Fig. 9. Two polygraph curves, taken from CASE 6, on October the 14th and the 23rd. The upper curve was taken during the paroxysm and when the ventricular rate had slowed in response to strophanthin. The lower curve was taken after the resumption of the normal rhythm.

CASE 7, F. D., a woman, aged 26. Auricular fibrillation. Mitral stenosis (non-rheumatic). Great improvement in general condition, slowing of the heart with diuresis following the administration of strophanthin.

Admitted on October the 12th, 1911, complaining of shortness of breath, throbbing in the neck, palpitation and giddiness.

Family history. Her father, mother, one brother and five sisters are all alive and healthy.

Previous illnesses. She was well up to the age of 13, but then became very anæmic and was at times unable to do her work owing to shortness of breath. She was admitted to Victoria Park Hospital in 1902 and again in 1903 and was found to be suffering from mitral stenosis. At this time her pulse was regular, the apex beat was inside the nipple line; a presystolic thrill, presystolic and systolic murmurs were present at the apex. There was œdema of the bases of both lungs but not of the feet. Since then she has been in moderate health, but at times has been unable to do her work owing to shortness of breath. There is no history of rheumatism or chorea.

History of present illness. She woke up suddenly at 3.30 a.m. one morning in July, 1911, with a feeling of great weakness and a distressing throbbing sensation in the neck. Since then she has become gradually worse.

Condition on admission. The patient sits propped up in bed. Her complexion is pale and rather yellow, and there are dark rings under the eyes. The lips are cyanosed and there is a considerable amount of visible and palpable pulsation at the root of the neck, which prevents her from sleeping. She has a troublesome cough with some expectoration. Her appetite is bad and the taking of any but the lightest food produces a feeling of sickness. The apex beat is in the sixth left interspace almost in the mid-axillary line; a thrill is felt on palpation. A marked heaving impulse of the left side of the chest occurs with each heart beat. The deep cardiac dullness extends $1\frac{1}{2}$ inches to the right and $7\frac{3}{4}$ inches to the left of the mid-sternum. The heart's action is very rapid and irregular. A loud presystolic bruit is present at the apex and the pulmonic second sound is accentuated. The pulse is scarcely palpable. The liver is palpable three fingerbreadths below the right costal margin. There is extensive œdema of the bases of the lungs, of the feet, and over the sacrum; there is slight ascites. The urine is scanty and contains a trace of albumen. Polygraphic tracings show the ventricular form of venous pulse and gross irregularity of the heart beat.

Treatment and progress. The patient remained in bed until October the 16th (four days), when she was given five separate injections of 1/500 grain of strophanthin at intervals of 1 hour. The ventricular rate fell from 162 per minute at 10.10 a.m. to 96 per minute at 5 p.m., a fall of 66 beats per minute in 7 hours (see Fig. 2). At the same time the condition of the patient improved greatly; she felt better, the dyspnoea diminished, and she slept all night and the greater part of the next day. On October the 17th two injections of 1/500 grain each were given at 12.27 p.m. and 1.32 p.m. respectively and 1/250 grain at 3.50 p.m. As a result, the ventricular rate fell from 124 to 86 per minute, a fall of 38 beats, between 12.15 p.m. and 7 p.m. ($6\frac{3}{4}$ hours). Diuresis occurred on October the 18th and the 19th and the patient passed as much as 128 ounces of urine within the space of 24 hours. On examination on October the 19th, the pulsation in the neck had disappeared, and there was only slight pulsation perceptible in the left intercostal spaces. She could now lie flat in bed without discomfort. Her appearance had improved and the cyanosis had disappeared. At the apex there was a bruit filling the whole of diastole. The liver had not decreased in size and œdema of the bases of the lungs and over the sacrum was still present. Her condition steadily improved and she slept and ate well. On October the 26th there was a very soft systolic bruit at the apex, the first sound was accentuated and the diastolic murmur had become early diastolic in time. The thrill at the apex was diastolic in time. The enlargement of the liver had somewhat decreased. The œdema had vanished from over the sacrum but was still present to a slight extent round the ankles. By November the 2nd the œdema of the lungs and feet had disappeared. The ventricular rate gradually quickened until on November the 6th it was 162 per minute. At the same time she complained of a return of the palpitation. She was pale, restless, dyspnoic and sleepless. On November the 7th she was given 1/250 grain of strophanthin at 10.7 a.m. and 1/500 grain at 1.7 p.m. As a result of these two injections the ventricular rate fell from 160 to 96 per minute, a fall of 64 beats per minute in $3\frac{1}{2}$ hours (illustrated by Fig. 5 and 6. A conspicuous improvement in the patient's condition took place and she slept well during the night. Pain, lasting from one to two hours, occurred at the sites of injection. There was slight œdema over the sacrum on November the 9th but otherwise the physical signs remained unchanged. After this the ventricular rate gradually increased and it was 150 per minute on November the 23rd while at the same time the patient felt ill. The liver was palpable four fingerbreadths below the right costal margin and was markedly pulsatile. There was œdema of the bases of both lungs. Tincture of digitalis in 15 minim doses given four times daily was commenced on November the 27th, and the ventricular rate rapidly fell and an anchoring of the patient's symptoms took place. The digitalis was discontinued on December the 3rd, a total of 7 drachms having been taken. The enlargement of the liver became less marked and on December the 7th it was palpable two fingerbreadths below the right costal margin and a further decrease in size took place during the next two weeks but it could still be felt just below the right costal margin at the time of her discharge from the hospital. The

ventricular rate had increased to over 90 per minute when the patient was discharged on December the 21st. At no time was there any decrease in the extent of deep cardiac dulness other than could be attributed to percussion error. The polygraphic tracings showed the ventricular form of venous pulse and gross irregularity of the heart beats throughout the period of observation.

TABLE VIII. (CASE 7.)

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
Oct.						
13th	10 a.m.	170			11-7 $\frac{1}{4}$	Orthopnoea. Sickness.
	2 p.m.	158				
	6 p.m.	171				
14th	10 a.m.	170		25+	7-7 $\frac{1}{4}$	Dyspnoea. Pulsation in neck.
	2 p.m.	166				Did not sleep well last night.
	8 p.m.	156				
15th	2 p.m.	162		25		
	6 p.m.	168				
16th	9.30 a.m.	162		28	1-7	Considerable pulsation in neck. Orthopnoea. Vomiting. Sleepless.
	10.10 a.m.		Stroph. 1/500 gr.			
	10.12 a.m.	160				
	10.15 a.m.	154				
	10.30 a.m.	150				
	10.45 a.m.	140				
	11 a.m.	154				
	11.11 a.m.		Stroph. 1/500 gr.			
	11.15 a.m.	146				
	11.30 a.m.	140				Sleepy. Can lie flat without discomfort. Patient says that "her heart has not been so quiet for weeks."
	11.45 a.m.	138				
	12 noon	132				
	12.10 p.m.		Stroph. 1/500 gr.			
	12.15 p.m.	126				
	12.30 p.m.	120				
	12.45 p.m.	124				
	1 p.m.	118				
	1.11 p.m.		Stroph. 1/500 gr.			
	1.15 p.m.	118				
	1.30 p.m.	116				
	1.45 p.m.	122				
	2 p.m.	122				
	2.10 p.m.		Stroph. 1/500 gr.			
	2.15 p.m.	124				
	2.30 p.m.	114				
	2.45 p.m.	110				Patient slept while tracing taken.
	3 p.m.	104				Patient slept while tracing taken.
	3.15 p.m.	106				
	3.30 p.m.	104				
	3.45 p.m.	102				
	4 p.m.	102				
	4.15 p.m.	100				
	4.30 p.m.	124				Sitting up and having tea
	4.45 p.m.	100				
	5 p.m.	96				
	5.15 p.m.	96				
	5.30 p.m.	96				
	5.45 p.m.	110				
	6 p.m.	102				
	6.15 p.m.	98				
	6.30 p.m.	98				
	6.45 p.m.	106				
	7 p.m.	94				
	7.15 p.m.	106				
	7.30 p.m.	100				

DATE	HOUR AT WHICH FRAGRING TAKEN.	HEART RATE PER MIN.	DRUG	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS
Oct. 16th	7.45 p.m.	96				
	8 p.m.	110				
	8.15 p.m.	108				Feels very much better. Can lie flat without discomfort. Throbbing in neck has disappeared.
17th	10.15 a.m.	116		16		
	12 noon	120				
	12.15 p.m.	124				Slept well all night. Feels very much better.
	12.27 p.m.		Stroph. 1.500 gr.			Great improvement in appearance.
	12.30 p.m.	122				
	12.45 p.m.	110				
	1 p.m.	126				
	1.15 p.m.	124				
	1.32 p.m.		Stroph. 1.500 gr.			
	1.45 p.m.	126				
	2 p.m.	118				
	2.15 p.m.	124				
	2.30 p.m.	134				
	2.45 p.m.	134				
	3 p.m.	116				
	3.15 p.m.	112				Slept during the greater part of the day.
	3.35 p.m.	136				
	3.45 p.m.	126				
	3.50 p.m.		Stroph. 1.250 gr.			
	4 p.m.	122				
	4.15 p.m.	120				
	4.30 p.m.	114				
	4.45 p.m.	102				
	5 p.m.	100				
	5.15 p.m.	122				
	5.30 p.m.	116				
	5.45 p.m.	102				
	6 p.m.	102				
	6.15 p.m.	96				Evening temperature 100.6° F.
	6.30 p.m.	88				
	6.45 p.m.	90				
	7 p.m.	86				
	7.15 p.m.	94				
	7.30 p.m.	90				
	7.45 p.m.	96				
	8 p.m.	98				
	8.15 p.m.	86				
	9 p.m.	98				
18th	10.15 a.m.	88		20		Slept well.
	2 p.m.	98				
	6 p.m.	84				
19th	10 a.m.	88		128	1 1/4	Oedema of bases of both lungs and over sternum. No pulsation in neck. No dyspnoea. Feels well.
	8.15 p.m.	94				
20th	10 a.m.	98		38		
	6 p.m.	100				
21st	10.15 a.m.	98		46		
	2 p.m.	94				
	6 p.m.	98				
22nd	2 p.m.	108		50		
	6 p.m.	98				
23rd	10 a.m.	94		42		
	6 p.m.	90				
24th	10.5 a.m.	96		42		
	8.15 p.m.	106				
25th	10 a.m.	106		46		
	6.10 p.m.	108				

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
Oct. 26th	10 a.m.	110		52	1½ 6¼	Feels well. No edema of feet. Slight edema over sacrum. Sleeping well
	1.45 p.m.	108				
	8.30 p.m.	104				
27th	10 a.m.	96		44		
	6 p.m.	110				
28th	10 a.m.	118		44		
	6.40 p.m.	104				
29th	6.30 p.m.	118		34		
30th	10 a.m.	100		32		
	2 p.m.	124				
	6 p.m.	118				
31st	10 a.m.	130		27		
	8 p.m.	116				
Nov. 1st	10 a.m.	148		28		
	6.15 p.m.	130				
2nd	10.5 a.m.	126		42	1½ 5¼	Feels well. Oedema disappeared. Up 1 hour in chair.
	2 p.m.	146				Up 1 hour.
	8.40 p.m.	134				
3rd	10 a.m.	132		29		
	6.45 p.m.	128				
4th	10.5 a.m.	156		45		Did not sleep well last night. Does not feel so well. Some pulsation in neck and throbbing in abdomen. Vomited. Up 1 hour. Felt better in evening.
	8.10 p.m.	148				
5th	2 p.m.	136		29		Up 1 hour. Slight rise of temperature in the evening (99.4° F.).
	6 p.m.	154				
6th	10 a.m.	146		31		Not feeling well. Throbbing in neck at times. Occasional sickness. Slept badly.
	2 p.m.	158				
	6 p.m.	162				
7th	9.15 a.m.	164		38	1-6	Slept better last night. Orthopnoea. Vomited in morning.
	9.45 a.m.	152				
	10.7 a.m.	160				
	10.7 a.m.		Stroph. 1/250 gr.			
	10.15 a.m.	142				
	10.30 a.m.	136				
	10.45 a.m.	124				
	11 a.m.	134				
	11.15 a.m.	118				
	11.30 a.m.	110				
	11.45 a.m.	112				
	12 noon	116				
	12.15 p.m.	108				
	12.30 p.m.	108				
	12.45 p.m.	108				
	1.7 p.m.		Stroph. 1/500 gr.			
	1.7 p.m.	108				
	1.15 p.m.	108				
	1.30 p.m.	102				Feeling very much better.
	1.45 p.m.	96				
	2 p.m.	98				
	2.15 p.m.	106				Pain at site of injection.
	3.45 p.m.	100				
	4 p.m.	94				
	4.15 p.m.	96				
	4.30 p.m.	104				
	4.45 p.m.	100				
	5 p.m.	102				
	5.15 p.m.	94				
	5.30 p.m.	98				
	5.45 p.m.	120				

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
Nov.						
7th	6 p.m.	94				
	6.15 p.m.	104				
	6.45 p.m.	102				
	8 p.m.	110				
8th	10 a.m.	130		30		Slept well last night.
	6 p.m.	102				
9th	10 a.m.	96		36	1½-6½	Slight oedema over sacrum
	8 p.m.	94				Slept well.
10th	10 a.m.	90		32		
	2.20 p.m.	106				
	6 p.m.	138				
11th	10 a.m.	100		28		
	2 p.m.	120				
	6 p.m.	112				
12th	2 p.m.	96		34		
	6.20 p.m.	126				
13th	10 a.m.	114		30		
	2 p.m.	100				
	6 p.m.	112				
14th	11 a.m.	106		32		Up 1 hour in chair.
	2 p.m.	106				
	8 p.m.	126				
15th	10 a.m.	96		34		Up 1 hour.
	6 p.m.	118				
16th	10 a.m.	102		42	1½-6½	Up 1 hour.
	2.10 p.m.	108				
	8.30 p.m.	130				
17th	9.55 a.m.	110		47		Up 1 hour.
	6.15 p.m.	112				
18th	10 a.m.	118		38		Up 1 hour.
	2 p.m.	130				
	8 p.m.	150				
19th	5.35 p.m.	128		32		Up 1 hour.
20th	10 a.m.	132		26		Up 2 hours.
	6 p.m.	134				
21st	10 a.m.	138		22		Up 2 hours.
	8.35 p.m.	152				
22nd	10 a.m.	148		36		Up 2 hours.
	2 p.m.	136				
	5.45 p.m.	148				
23rd	10 a.m.	132		32	1½-5½	Not looking quite so well. Sleeping well. Liver enlarged and pulsatile.
	8.10 p.m.	150				
24th	10 a.m.	134		28		Up 2 hours.
	6 p.m.	154				
25th	10.10 a.m.	158		36		Up 2 hours. Slept badly last night.
	8 p.m.	158				
26th	2 p.m.	154		32		Slept badly last night.
	6 p.m.	136				Up 2 hours.
27th	10 a.m.	156		26+		Feels throbbing in left side of chest. Slept badly.
	2.30 p.m.	146				
	6.10 p.m.	132	Tr. Digitalis 1 dr.			Looks ill Bed.
28th	10 a.m.	98		28+		Feeling better
	2 p.m.	84				
	8 p.m.	90	Tr. Digitalis 1 dr.			
29th	10 a.m.	80		30		Slept well.
	6.30 p.m.	90	Tr. Digitalis 1 dr.			
30th	10 a.m.	68		28	2-6½	Feels very well.
	8.40 p.m.	78	Tr. Digitalis. 1 dr.			Up 1 hour.
Dec.						
1st	10 a.m.	76		34+		Up 1 hour.
	8.15 p.m.	66	Tr. Digitalis 1 dr.			

DATE	HOUR AT WHICH TRACING TAKEN.	HEART RATE PER MIN.	DRUG.	URINE (IN OZS.)	SIZE (IN INCHES).	REMARKS.
Dec.						
2nd	11.25 a.m.	64	Tr. Digitalis 1 dr.	32		Up 1 hour.
3rd	6 p.m.	102	Tr. Digitalis 1 dr. (Total taken = 7 drachms)	48		Up 1 hour.
4th	10 a.m.	74		59		Up 1 hour.
	8.10 p.m.	70				
5th	10 a.m.	88		34		Up 1 hour.
	8 p.m.	80				
6th	10 a.m.	82		30		Up 2 hours.
	6.25 p.m.	90				
7th	10 a.m.	74		28	1½ 6	Up 2 hours.
	8 p.m.	88				
8th	10 a.m.	80		30		Up 2 hours.
	6.20 p.m.	92				
9th	10 a.m.	80		30		Up 2 hours.
	6 p.m.	96				
10th	2 p.m.	112		44		Up 2 hours.
	6 p.m.	100				
11th	10 a.m.	84		38		Up 3 hours.
	7.55 p.m.	86				
12th	10 a.m.	96		36		Up 3 hours.
	8 p.m.	102				
13th	10 a.m.	80		36		Up 4 hours.
	6.45 p.m.	94				
14th	10.10 a.m.	94		32	1-6½	Feels well.
	9.20 p.m.	118				
15th	10 a.m.	84		32		Up 4 hours.
	8 p.m.	88				
16th	10 a.m.	76		32		Up 4 hours.
	8.30 p.m.	130				
17th	7.35 p.m.	104		38		Up 4 hours.
18th	10 a.m.	78		40		Up 5 hours.
19th	10 a.m.	90		46		
	8 p.m.	96				
20th	10 a.m.	110		36		
	8.10 p.m.	126				
21st	10.15 a.m.	88		42	1½ 6½	Appearance healthy. No dyspnoea. Feels well.

Discharged on December the 21st, 1911.

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